U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

SEARCH REQUEST FORM

Requestor's Name: Cook

Serial Number: 09/009213 et al

Date: 10/19/98 Phone: 308 4724 Art Unit: 1614

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).

Styczynski, Peter is applicant.

For a series of cases directed to 1) increasing hair growth by increasing metabolism of androgens which cause alopecia 2) decreasing hirsutism by increasing metabolism of androgens which cause alopecia please search for

I - a reference teaching the role of androgens in 1) and 2) above; dated earlier than 1997.

II - kinds of all enzymes known to metabolize androgens that use 1) & 2) above to their inactive forms, such as UGT, sulfotransferases, etc.

Thanks
Rebecca

III - any compounds known to induce said enzymes.

IV - Please provide the structures for the attached Compounds of claims 3-16.

STAFF USE ONLY

Date completed: 10-29-98
Searcher: JDH-1
Terminal time:
Elapsed time:
CPU time:
Total time:
Number of Searches:
Number of Databases:

Search Site
- STIC
- CM-1
- Pre-S

Type of Search
- N.A. Sequence
- A.A. Sequence
- Structure
- Bibliographic

Vendors
- IG
- STN
- Dialog
- APS
- Geninfo
- SDC
- DARC/Questel
- Other

PTO-1590 (9-90)

I

=> d bib abs 123 1-10

L23 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 1998 ACS
AN 1996:708970 HCAPLUS
DN 126:14804
TI **Androgen metabolism** as it affects **hair growth** in **androgenic** alopecia
AU Kaufman, Keith D.
CS Merck Research Laboratories, Clinical Research, Rahway, NJ, USA
SO Dermatol. Clin. (1996), 14(4, Update on Hair Disorders), 697-711
CODEN: DRMCDJ; ISSN: 0733-8635
PB Saunders
DT Journal; General Review
LA English
AB A review, with 67 refs., which discusses: androgen physiol.; androgenic alopecia; pathophysiol. of hormonal factors in androgenic alopecia; androgen metab. within skin; and studies with 5.alpha.-reductase inhibitors.

L23 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 1998 ACS
AN 1996:360274 HCAPLUS
DN 125:26555
TI The metabolism of testosterone by dermal papilla cells cultured from human pubic and axillary hair follicles concurs with hair growth in 5.alpha.-reductase deficiency
AU Hamada, Kazuto; Thornton, Margaret Julie; Laing, Ian; Messenger, Andrew Guy; Randall, Valerie Anne
CS Department of Biomedical Sciences, University of Bradford, Bradford, UK
SO J. Invest. Dermatol. (1996), 106(5), 1017-1022
CODEN: JIDEAE; ISSN: 0022-202X
DT Journal
LA English
AB Androgens regulate the growth of many human hair follicles, but only public, axillary, and scalp hair growth occur in men with 5.alpha.-reductase deficiency. This suggests that 5.alpha.-dihydrotestosterone is the active intracellular androgen in androgen-dependent follicles, except in the axilla and pubis. Since the dermal papilla plays a major regulatory role in hair follicles and may be the site of androgen action, we have investigated androgen metab. in six primary lines of cultured dermal papilla cells from public and axillary hair follicles; previous studies have shown that beard cells take up and metabolize testosterone, retaining and secreting 5.alpha.-dihydrotestosterone. After 24 h preincubation in serum-free Eagle's medium 199, 100-mm dishes of confluent cells were incubated for 2 h with 5 nM [1,2,6,7-3H]testosterone. Media were collected and the cells washed with phosphate-buffered saline and extd. with chloroform:methanol (2:1). After the addn. of unlabeled and 14C-labeled marker steroids, the exts. were analyzed by a two-step thin-layer chromatog. system; steroid identity was confirmed by recrystn. to a const. 3H/14C ratio. Beard and public dermal papilla cells were also incubated for 24 h, and the medium was analyzed at various times. The results from pubic and axillary primary cell lines were similar. In both cells and media the major steroid identified was testosterone, but significant amts. of androstenedione were present, indicating 17.beta.-hydroxysteroid dehydrogenase activity;

androstanedione was also identified within the cells, but a small amt. of 5.alpha.-dihydrotestosterone was only identified in one pubic cell line. Beard dermal papilla cells secreted large amts. of 5.alpha.-dihydrotestosterone into the medium over 24 h in contrast to pubic cells, which produced only very small amts. The pubic and axillary cell results contrast with the observations of pronounced 5.alpha.-dihydrotestosterone in beard cells and confirm that androgen metab. in cultured dermal papilla cells reflects the parent follicle's ability to respond to androgen in the absence of 5.alpha.-reductase type II in vivo. This supports our hypothesis that androgen acts on hair follicles via the dermal papilla and suggests that cultured dermal papilla cells may offer an important model system for studies of androgen action.

L23 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 1998 ACS
AN 1995:542753 HCAPLUS
DN 122:273734
TI Male pattern baldness and hair growth promoters
AU Yokoyama, Daisaburo
CS Biol. Sci. Res. Center, Lion Corporation, Kanagawa-ken, 256, Japan
SO Yukagaku (1995), 44(4), 266-73
CODEN: YKGKAM; ISSN: 0513-398X
DT Journal; General Review
LA Japanese
AB This article reviews with 45 refs. hair growth and the cycle, male pattern baldness and its cause, hair growth promoters, and the evaluation methods for such promoters. The mechanism of hair growth and causes of male pattern baldness are still not clear, but recent studies on hair growth are bringing up some interesting and important facts. New discoveries on energy **metab.**, interaction between hair matrix and dermal papilla, and action of **androgens** are discussed along with their application to the prodn. of new **hair growth** promoters. A new hair growth promoter, monopentadecanoylglycerol (PDG), is discussed in relation to its effect for promoting energy metab.

L23 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 1998 ACS
AN 1994:125283 HCAPLUS
DN 120:125283
TI Differences in testosterone metabolism by beard and scalp hair follicle dermal papilla cells
AU Thornton, M. J.; Laing, I.; Hamada, K.; Messenger, A. G.; Randall, V. A.
CS Dep. Biomed. Sci., Univ. Bradford, Bradford/West Yorks, BD7 1DP, UK
SO Clin. Endocrinol. (Oxford) (1993), 39(6), 633-9
CODEN: CLECAP; ISSN: 0300-0664
DT Journal
LA English
AB Androgens have paradoxically different effects on hair follicles depending on body site, stimulating beard growth while inducing regression in some areas of the scalp. The mesenchyme derived dermal papilla at the base of the hair follicle regulates many aspects of growth of follicular epithelium, and is probably the site of androgen action. Since 5.alpha.-dihydrotestosterone is considered to be the active intracellular androgen in many target tissues and is required for some **androgen**-mediated **hair growth**, such **androgen**-sensitive cells should contain 5.alpha.-reductase and whether the **metabolic** capacity varies with the body site of the follicle

in line with the clin. picture. Testosterone metab. in cultured dermal papilla cells from androgen sensitive beard follicles was compared with less androgen dependent non-balding scalp follicles. Primary cell cultures were established from follicles of 11 patients with normal hair growth. The cells were grown to confluence in 10-cm Petri dishes and incubated with 5 nm 3H-testosterone in serum-free medium for 2 h. The cells and the culture medium were collected sep. for individual anal. Unlabeled carrier and 14C-marker steroids were added to both the cell and medium exts. before sepn. by thin-layer chromatog. The individual steroid identities were confirmed by recrystalizing up to five time to a const. 3H/14C ratio. Testosterone was taken up by both cell types; significant amts. of 5.alpha.-dihydrotestosterone were recovered inside beard cells, but not in scalp cells, whereas androstenedione was identified in both. An unidentified compd. was present intracellularly in both cell types, but was not present in the culture medium. 5.alpha.-Dihydrotestosterone was present only in the culture medium of beard cells but androstenedione was present in a similar amt. in the medium from both cell types. The presence of other steroids could not be confirmed in either the cell exts. or the culture medium. The prodn. of 5.alpha.-dihydrotestosterone by beard cells concurs with the poor beard growth in men with 5.alpha.-reductase deficiency, supporting the authors' hypothesis that androgens mediate their effects on the hair follicle via the mesenchyme-derived dermal papilla.

L23 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 1998 ACS
AN 1991:670946 HCAPLUS
Correction of: 1991:550857
DN 115:270946
Correction of: 115:150857
TI Clinical and biochemical parameters of androgen action in normal healthy caucasian versus Chinese subjects
AU Lookingbill, Donald P.; Demers, Laurence M.; Wang, Christina; Leung, Andrew; Rittmaster, Roger S.; Santen, Richard J.
CS Coll. Med., Pennsylvania State Univ., Hershey, PA, 17033, USA
SO J. Clin. Endocrinol. Metab. (1991), 72(6), 1242-8
CODEN: JCEMAZ; ISSN: 0021-972X
DT Journal
LA English
AB Stimulation of androgen-sensitive hair follicles is mediated by dihydrotestosterone (DHT) formed in these tissues by 5.alpha.-redn. of testosterone. Mechanisms for increased body hair in some human populations may involve 5.alpha.-reductase activity, resulting in elevated tissue levels of DHT. This finding could have other important clin. implications since 5.alpha.-reductase is pivotal in the pathophysiol. of prostatic disease. Caucasian and Chinese subjects were compared for chest hair d. and serum levels of androgen precursors and 5.alpha.-reduced androgen metabolites. Mean chest hair scores (using a scale of 0-4) were 3.0 vs. 0.8 in caucasian vs. Chinese. Levels of 5.alpha.-reduced androgen products were also strikingly higher in the caucasian vs. Chinese subjects. Serum 3.alpha.-androstanediol glucuronide levels were 34.7 vs. 19.7 nM for the men and 21.5 vs. 9.4 nM for the women. Serum levels of androsterone glucuronide were 179 vs. 107 nM for the caucasian vs. Chinese men and 173 vs. 81 nM for the women. Serum levels of total and bioavailable testosterone did not differ between the racial groups, but serum levels of the precursor androgens, dehydroepiandrosterone sulfate and androstenedione, were higher in

the caucasian vs. Chinese men, but not in the women. Increased serum levels of 5.alpha.-reduced androgen metabolites in caucasians vs. Chinese subjects provide circumstantial evidence for a racial difference in 5.alpha.-reductase activity and suggest a mechanism for the increased body hair obsd. in the caucasian men. Increased levels of precursor androgens may also play a role.

L23 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 1998 ACS
AN 1991:550857 HCAPLUS
DN 115:150857
TI Clinical and biochemical parameters of androgen action in normal healthy caucasian versus Chinese subjects
AU Lookingbill, Donald P.; Demers, Laurence M.; Wang, Christina; Leung, Andrew; Rittmaster, Roger S.; Santen, Richard J.
CS Coll. Med., Pennsylvania State Univ., Hershey, PA, 17033, USA
SO J. Clin. Endocrinol. Metab. (1991), 27(6), 1242-8
CODEN: JCEMAZ; ISSN: 0021-972X
DT Journal
LA English
AB Stimulation of androgen-sensitive hair follicles is mediated by dihydrotestosterone (DHT) formed in these tissues by 5.alpha.-redn. of testosterone. Mechanisms for increased body hair in some human populations may involve 5.alpha.-reductase activity, resulting in elevated tissue levels of DHT. This finding could have other important clin. implications since 5.alpha.-reductase is pivotal in the pathophysiol. of prostatic disease. Caucasian and Chinese subjects were compared for chest hair d. and serum levels of androgen precursors and 5.alpha.-reduced androgen metabolites. Mean chest hair scores (using a scale of 0-4) were 3.0 vs. 0.8 in caucasian vs. Chinese. Levels of 5.alpha.-reduced androgen products were also strikingly higher in the caucasian vs. Chinese subjects. Serum 3.alpha.-androstanediol glucuronide levels were 34.7 vs. 19.7 nM for the men and 21.5 vs. 9.4 nM for the women. Serum levels of androsterone glucuronide were 179 vs. 107 nM for the caucasian vs. Chinese men and 173 vs. 81 nM for the women. Serum levels of total and bioavailable testosterone did not differ between the racial groups, but serum levels of the precursor androgens, dehydroepiandrosterone sulfate and androstenedione, were higher in the caucasian vs. Chinese men, but not in the women. Increased serum levels of 5.alpha.-reduced androgen metabolites in caucasians vs. Chinese subjects provide circumstantial evidence for a racial difference in 5.alpha.-reductase activity and suggest a mechanism for the increased body hair obsd. in the caucasian men. Increased levels of precursor androgens may also play a role.

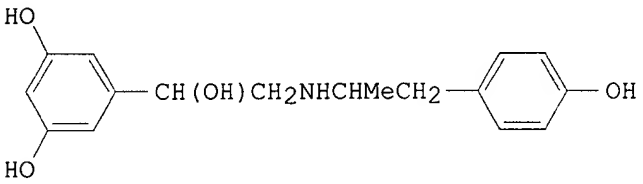
L23 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 1998 ACS
AN 1984:21184 HCAPLUS
DN 100:21184
TI **Androgen metabolism** by isolated hairs from women with idiopathic **hirsutism** is usually normal
AU Glickman, Sally P.; Rosenfield, Robert L.
CS Pritzker Sch. Med., Univ. Chicago, Chicago, IL, 60637, USA
SO J. Invest. Dermatol. (1984), 82(1), 62-6
CODEN: JIDEAE; ISSN: 0022-202X
DT Journal
LA English
AB The hypothesis that idiopathic hirsutism (IH) may be due to abnormality of androgen-responsive hair follicles was tested. Because androgen metab. within target cells is an important

determinant of androgen action, the rates of formation and disposition of the major mediators of androgen action, testosterone (T) and dihydrotestosterone (DHT), were analyzed. In normal women, the pattern of **androgen metab.** by **growing hairs** favors T predominance over DHT and inactivation of both these 17.beta.-hydroxysteroids to 17-ketosteroids. This pattern results greatly from predominance of 17.beta.-hydroxysteroid dehydrogenation. In normal women's scalp hair, DHT disposition to 5.alpha.-androstanedione proceeded at the rate of 8.6%/.mu.g DNA/min, whereas DHT was formed from T at a rate of 0.14, and T was formed from androstenedione at a rate of 0.60, all significantly different from one another. Both the formation of 17-ketosteroids and the apparent 5.alpha.-reductase activity were exaggerated in the pubic hair of men; whether these differences are site-, sex-, or androgen-related, remains to be detd. Pubic hairs tended to metabolize androgens at a greater rate than did scalp hair. This was related to the significantly greater DNA content of plucked pubic hairs, a difference unrelated to sex or androgen levels. Women with IH had heterogeneous pubic hair abnormalities. Only 1 of the 4 IH patients studied had abnormal pubic hair follicle androgen metab., with the greatest abnormality being exaggerated rate of 17.beta.-hydroxysteroid inactivation to 17-ketosteroids. Two of the other 3 IH cases had increased DNA content of plucked pubic hairs, a different kind of exaggeration of normal, which suggests an abnormality of hair follicle growth unrelated to androgen sensitivity. The concept that IH is related to various distinct types of sexual hair abnormalities which reflect fundamental defects in the regulation of hair growth is suggested.

L23 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 1998 ACS
AN 1982:97972 HCAPLUS
DN 96:97972
TI Androgen metabolism in isolated human hair roots
AU Schweikert, H. U.; Wilson, J. D.
CS Med. Univ. Poliklin., Bonn, Fed. Rep. Ger.
SO Hair Res., [Proc. Int. Congr.], 1st (1981), Meeting Date 1979, 210-14. Editor(s): Orfanos, Constantin E.; Montagna, William,; Stuettgen, Guenter. Publisher: Springer, Berlin, Fed. Rep. Ger. CODEN: 47BGAO
DT Conference
LA English
AB To investigate the relation between **androgens** and **hair growth** the **metab.** of 3H-labeled testosterone [58-22-0] and 3H-labeled androstenedione [63-05-8] was assessed in isolated human **hair** roots. To quantitate androgen metab. in only a few hair roots, a micromethod was developed. Using this method, it was shown that both growing (anagen) and resting (telogen) hair roots originating from 10 different body sites contain 2 major enzymic systems namely 5.alpha.-reductase [9036-43-5] and 17.beta.-hydroxy steroid dehydrogenase [9015-81-0]. No significant relation was found, with either testosterone or androstenedione as a substrate, between the **androgen**-mediated **growth** of **hair** and the capacity to form 5.alpha.-**metabolites**. However, a significantly greater formation of 5.alpha.-androstanes was found in the frontal area of balding men than in the same area in nonbalding men. Since 5.alpha.-redn. is irreversible and the formation of 17-keto steroids is favored, androstanedione is the principal intracellular androgen in human hair roots. The complex enzymic

machinery required to aromatize androstenedione to estrone [53-16-7] in human hair roots was shown.

L23 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 1998 ACS
AN 1981:400679 HCAPLUS
DN 95:679
TI Increased hair growth during prolonged tocolytic therapy with Fenoterol. Measurements of testosterone, androstanediol, cortisol and ACTH
AU Spaetling, L.; Schneider, H.; Staehler, E.; Daume, E.; Sturm, G.
CS Univ. Frauenklin. Marburg, Marburg, Fed. Rep. Ger.
SO Geburtshilfe Frauenheilkd. (1980), 40(11), 1022-8
CODEN: GEFRA2; ISSN: 0016-5751
DT Journal
LA German
GI



I

AB Prolonged tocolytic (premature parturition inhibition) therapy with fenoterol (I) [13392-18-2] in humans increased hair growth all over the skin. This effect was not due to an increase in androgen metabolites since plasma testosterone [58-22-0] levels were decreased and androstanediol [571-20-0] showed a slight rise the 3rd wk of therapy after an initial fall. I did not affect plasma ACTH [9002-60-2] or cortisol [50-23-7] levels.

L23 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 1998 ACS
AN 1974:458490 HCAPLUS
DN 81:58490
TI Regulation of human hair growth by steroid homones. I. Testosterone metabolism in isolated hairs
AU Schweikert, Hans U.; Wilson, Jean D.
CS Southwest. Med. Sch., Univ. Texas, Dallas, Tex., USA
SO J. Clin. Endocrinol. Metab. (1974), 38(5), 811-19
CODEN: JCEMAZ
DT Journal
LA English
AB 4-Androstene-3,17-dione [63-05-8], 5.alpha.-androstane-3,17-dione [846-46-8], and 17.beta.-hydroxy-5.alpha.-androstan-3-one [521-18-6] were the major metabolites of testosterone (I) [58-22-0] after incubation with isolated hair roots. Scalp hair of women performed 5.alpha.-redn. to approx. the same degree as beard hair from men. The formation of 17-keto metabolites was lower in telogen hairs than in anagen hairs from all body sites, whereas the formation of 17.beta.-hydroxy-5.alpha.-androstan-3-one was lower in telogen hairs only from the scalp. In general a higher formation of 5.alpha.-reduced metabolites and 17-keto steroid metabolites was obsd. at all sites of the scalp of bald men as compared to hair obtained from the corresponding sites of women and nonbalding men,

and a significantly higher rate of metab. was found at the frontal area of the bald men. Regional difference in **androgen** -mediated **hair growth** may not be the result of variations in I **metab**. in the **hair** follicles.

=> d bib abs l24

L24 ANSWER 1 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1996:589853 HCAPLUS
DN 125:298284
TI PCOS (polycystic ovary syndrome) and androgen
AU Kitawaki, Jo; Yamamoto, Takara
CS Kyoto Prefect. Univ. Med., Kyoto, 602, Japan
SO Horm. Front. Gynecol. (1996), 3(3), 233-239
CODEN: HFGYFH; ISSN: 1340-220X
DT Journal; General Review
LA Japanese
AB A review, with 19 refs., on the abnormalities of steroid **metab.**, adrenal **androgen** excess and **hirsutism** in PCOS, and treatments of hyperandrogenic PCOS patients with oral contraceptives, cyproterone acetate etc.

=> d bib abs l24 2-36

L24 ANSWER 2 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1996:75148 HCAPLUS
DN 124:107063
TI 5.alpha.-Androstane-3.alpha.,17.beta.-diol and 5.alpha.-androstane-3.alpha.,17.beta.-diol-glucuronide in plasma of normal children, adults and patients with idiopathic hirsutism: a mass spectrometric study
AU Wudy, Stefan A.; Wachter, Ulrich A.; Homoki, Janos; Teller, Walter M.
CS First Dep. Pediatrics, Univ. Ulm, Germany
SO Eur. J. Endocrinol. (1996), 134(1), 87-92
CODEN: EJOEEP; ISSN: 0804-4643
DT Journal
LA English
AB The authors investigated the developmental patterns of 5.alpha.-androstane-3.alpha.,17.beta.-diol (AD) and 5.alpha.-androstane-3.alpha.,17.beta.-diol-glucuronide (ADG) in plasma of normal children and adults of both sexes and in patients with idiopathic hirsutism using a physicochem. method: high-resoln. gas chromatog./mass spectrometry (HRGC/MS). In children below the age of 11 yr, AD and ADG increased with age showing no differences between sexes (mean, nmol/L): normal subjects 3-6 yr: AD in females 0.08, in males 0.07; ADG in females 0.15, in males 0.14; normal subjects 7-10 yr: AD in females 0.17, in males 0.17; ADG in females 0.59, in males 0.47. Thereafter, AD and ADG showed a greater increase in males (normal subjects 11-15 yr: AD in females 0.24, in males 0.41; ADG in females 1.47, in males 3.36). In adults, plasma levels did not overlap between females and males (AD in females 0.24, in males 0.99; ADG in females 2.32, in males 13.01). 5.alpha.-Androstane-3.alpha.,17.beta.-diol-glucuronide discriminated better between sexes than AD. In idiopathic hirsutism, mean plasma concns. of AD and ADG were higher than those of healthy females (ages 11-15 yr: AD 0.31, ADG 3.48; ages > 16 yr: AD 0.44, ADG 6.46), but 54% of patients had normal plasma concns. of AD and 29% had normal ADG values. Thus, ADG reflected androgenicity better than AD. However, both **metabolites** were imperfect markers of **androgenicity** in idiopathic **hirsutism**. Therefore,

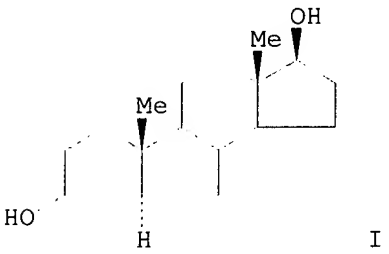
the findings do not support the concept of increased 5.alpha.-reductase activity in all patients with idiopathic hirsutism.

L24 ANSWER 3 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1994:601910 HCAPLUS
DN 121:201910
TI Hyperandrogenism, polycystic ovary syndrome, and hirsutism
AU Barnes, Randall B.
CS University Chicago, Chicago, IL, USA
SO Curr. Opin. Endocrinol. Diabetes (1994), 1ST ED., 200-5
CODEN: CENDES; ISSN: 1068-3097
DT Journal; General Review
LA English
AB A review with 46 refs. Disorders of androgen excess are among the most common reproductive endocrine abnormalities in women. Most cases of hyperandrogenism probably result from abnormal regulation of the androgen-forming enzymes in the ovary, adrenal, or both. This may be due to an intrinsic abnormality making the enzyme respond inappropriately to regulatory factors, or it may be secondary to excess or deficiency of endocrine factors such as LH or insulin or of paracrine or autocrine growth factors. Hyperandrogenism is assocd. with not only infertility and hirsutism but also insulin resistance, diabetes, and heart disease. Thus, its proper diagnosis and management is essential to the maintenance of good health. This review examines the sources, pathophysiol., long-term consequences, and therapy of androgen excess.

L24 ANSWER 4 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1994:454820 HCAPLUS
DN 121:54820
TI Role of endogenous estrogen in the hirsutism paradigm
AU Wild, Robert A.
CS Health Sci. Cent., Univ. Oklahoma, Oklahoma City, OK, 73126, USA
SO J. Reprod. Med. (1994), 39(4), 273-6
CODEN: JRPMAP; ISSN: 0024-7758
DT Journal; General Review
LA English
AB A review with 15 refs. The study of women with androgen excess as a biol. expt. in nature may improve the the understanding of hormonal determinants of cardiovascular risk. These women, who have androgen and estrogen excess, also have altered apolipoprotein metab., which correlates with insulin resistance. They often have android obesity, which appears to aggravate their metabolic alterations. Insulin resistance seems to have more of an influence on altered apolipoprotein **metab**. than does endogenous ovarian **androgen** or estrogen, at least in **hirsute** women who are obese. It is hypothesized that adrenal dehydroepiandrosterone sulfate may modify the effects of insulin resistance, as reflected in androgen and apolipoprotein lipid metab. These hormonal interactive influences, which require further investigation, may hold clues to why men and women differ in the time of onset of the multifactorial problem of coronary vascular disease.

L24 ANSWER 5 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1989:51492 HCAPLUS
DN 110:51492
TI Urinary 5.alpha.-androstane-3.alpha.,17.beta.-diol levels in normal

and hirsute women: discriminating power and relation to other urinary steroids
AU Muller, Lynette M.; Phillipou, George
CS Dep. Clin. Chem., Queen Elizabeth Hosp., Woodville, 5011, Australia
SO J. Steroid Biochem. (1988), 31(6), 979-82
CODEN: JSTBBK; ISSN: 0022-4731
DT Journal
LA English
GI



I

AB When urinary levels of 7 steroids, 5.alpha.-androstane-3.alpha.,17.beta.-diol (I), 5.beta.-androstane-3.alpha.,17.beta.-diol, androsterone, etiocholanolone, tetrahydrocortisone, tetrahydrocortisol, and allo-tetrahydrocortisol were measured in both normal and hirsute women, results confirmed I as the most significant steroid with respect to discrimination between hirsute and normal subjects. Investigation of the inter-steroid relationships, by using multivariate techniques, established that the mode of steroid metab. was different between the 2 groups. Whereas in normal women the strong correlation among all the **androgen metabolites** inferred a predominant hepatic route to I formation, the same analogy was not applicable to the **hirsute** subjects. Excellent agreement was found for the predicted vs. actual excretion of I in normal women, based on a regression model involving the 6 other steroids as independent variables. When the same model was used for estn. of I levels in 13 hirsute subjects, misclassified as normal, 50% gave values which were considerably less than actually measured. Evidently, this discrepancy with respect to these hirsute subjects is a reflection of extrahepatic prodn. of I due to increased 5.alpha.-reductase activity.

L24 ANSWER 6 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1986:527502 HCAPLUS
DN 105:127502
TI Dihydrotestosterone metabolism
AU Toscano, Vincenzo
CS Univ. La Sapienza, Rome, Italy
SO Clin. Endocrinol. Metab. (1986), 15(2), 279-92
CODEN: CEDMB2; ISSN: 0300-595X
DT Journal; General Review
LA English
AB A review, with 49 refs., on dihydrotestosterone [521-18-6], its **metabolite** 5.alpha.-androstan-3.alpha.,17.beta.-diol [1852-53-5], and the actions of these **androgens** on target tissues in normal and **hirsute** women.

L24 ANSWER 7 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1986:492056 HCAPLUS
DN 105:92056
TI **Androgen Metabolism** in **Hirsute** and Normal Females. [In: Clin. Endocrinol. **Metab.**, 1986; 15(2)]
AU Horton, R.; Lobo, R. A.; Editors
CS UK
SO (1986) Publisher: (W.B. Saunders Co., London, UK), 409 pp.
DT Book
LA English
AB Unavailable

L24 ANSWER 8 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1986:66920 HCAPLUS
DN 104:66920
TI Androstanediol glucuronide plasma clearance and production rates in normal and hirsute women
AU Greep, N.; Hoopes, M.; Horton, R.
CS Dep. Med., Univ. South. California, Los Angeles, CA, 90033, USA
SO J. Clin. Endocrinol. Metab. (1986), 62(1), 22-7
CODEN: JCEMAZ; ISSN: 0021-972X
DT Journal
LA English
AB The kinetics and metab. of tritiated 5.alpha.-androstane-3.alpha.-17.beta.-diol glucuronide (I) in normal and hirsute women were studied. No difference in the MCR of I between normal and hirsute women was found. The blood prodn. rate was markedly increased in hirsute women and correlated well with the plasma I level. In women, the conversion ratio of I to the unconjugated 3.alpha.-diol or dihydrotestosterone was <1%, while the conversion ratio to dihydrotestosterone glucuronide was .apprx.6%. Apparently, the elevated plasma levels of I characteristic of **hirsutism** reflect increased prodn. of this **androgen metabolite.**

L24 ANSWER 9 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1985:589999 HCAPLUS
DN 103:189999
TI Diagnosis of androgenization in women
AU Schmidt, H.
CS Fachbereich Endokrinol., Dtsch. Klin. Diagn., Wiesbaden, 6200, Fed. Rep. Ger.
SO Aerztl. Kosmetol. (1985), 15(4), 234-6, 239,40
CODEN: AEKODN; ISSN: 0340-5702
DT Journal; General Review
LA German
AB A review and discussion, with 1 ref., of the role of hormone detns. in indicating the causative nature of androgenization in women. In addn. to disturbances of ovarian and adrenal cortex steroid metab. (which may or may not be assocd. with tumors of these organs), hyperandrogenization of unknown origin and patients showing normal serum hormone levels are discussed.

L24 ANSWER 10 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1985:554409 HCAPLUS
DN 103:154409
TI The effect of spironolactone on genital skin 5.alpha.-reductase

activity
AU Serafini, Paulo C.; Catalino, Jerome; Lobo, Rogerio A.
CS Sch. Med., Univ. South. California, Los Angeles, CA, 90033, USA
SO J. Steroid Biochem. (1985), 23(2), 191-4
CODEN: JSTBBK; ISSN: 0022-4731
DT Journal
LA English
AB The effect of spironolactone (I) [52-01-7] on genital skin 5.alpha.-reductase [9036-43-5] activity (5.alpha.-RA) of hirsute women (HW) in vivo as well as in normal genital skin in vitro was evaluated. Thirteen HW (Ferriman-Gallwey score of 23.3) received 100 mg I twice a day for a month. Twenty-three nonhirsute women were selected as controls for the assessment of genital skin 5.alpha.-RA. I was added to incubations of genital skin from 9 addnl. controls in vitro in concns. of 1.2 .times. 10-8-10-5M. HW had significantly higher conversion ratios (CR) of testosterone (T) [58-22-0] to dihydrotestosterone (DHT) [521-18-6] compared with controls. Post treatment values for the CR of T to DHT were significantly lower than prior to I (17.5% and 8.05%) and the mass of DHT produced also decreased by 37%. The CR of T to 5.alpha.-androstane-3.alpha.,17.beta.-diol [1852-53-5] decreased by 30%. In 11 of 13 women, a redn. of 5.alpha.-RA was demonstrated, whereas the activity remained unchanged in the other 2 patients. The max. in vitro inhibitory effect of I on the CR of T to DHT occurred with a concn. of 1.2 .times. 10-5M. Evidently, I has a direct inhibitory effect on 5.alpha.-RA. The beneficial effect of I treatment in HW may be related, in part, to this inhibition of 5.alpha.-RA.

L24 ANSWER 11 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1984:488316 HCAPLUS
DN 101:88316
TI **Metabolism** and concentration of **androgenic** steroids in the abdominal skin of women with idiopathic **hirsutism**
AU Faredin, I.; Toth, I.
CS First Dep. Med., Univ. Med. Sch., Szeged, H-6701, Hung.
SO Acta Med. Hung. (1984), 41(1), 19-34
CODEN: AMEHDS
DT Journal
LA English
AB The abdominal skin of 3 women with idiopathic hirsutism contained increased concns. of androgens and increased enzymic capacity for androgen formation when compared with skin from healthy women. Blood levels of androgens were normal in 1 hirsute woman, indicating that her hirsutism was entirely attributable to the altered skin metab. Blood levels of 4-androstene-3,17-dione were above normal in the other 2 **hirsute** women, indicating that their **hirsutism** derived from a combination of altered skin **metab**. and high blood **androgen** levels.

L24 ANSWER 12 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1984:488315 HCAPLUS
DN 101:88315
TI **Metabolism** and concentration of **androgenic** steroids in abdominal skin of **hirsute** women with adrenogenital syndrome
AU Toth, I.; Faredin, I.
CS First Dep. Med., Univ. Med. Sch., Szeged, H-6701, Hung.

SO Acta Med. Hung. (1984), 41(1), 7-18
CODEN: AMEHDS
DT Journal
LA English
AB Two patients were studied. In one patient (with higher androgen overprodn.), more testosterone (Test.) than normal was formed from the precursors 3.beta.-hydroxy-5-androstene-17-one (DHA), 5-androstene-3.beta.,17.beta.-diol (.DELTA.5-diol), or 4-androstene-3,17-dione (.DELTA.4-dione), suggesting that the biosynthetic pathway involving 17.beta.-hydroxysteroid dehydrogenase and .DELTA.5-3.beta.-hydroxysteroid dehydrogenase was enhanced in the abdominal skin. Androgen formation was not increased in the less severely affected woman. The concns. of DHA, 3.alpha.-hydroxy-5.alpha.-androstane-17-one, .DELTA.4-dione, .DELTA.5-diol, Test., 17.beta.-hydroxy-5.alpha.-androstane-3-one, and C19-steroid sulfates were increased in the 2 patients as compared with healthy women. Apparently, hyperandrogenism exists in the skin of these patients.

L24 ANSWER 13 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1984:207421 HCAPLUS
DN 100:207421
TI Prolactin in hirsute women: possible roles for androgens in suppressing basal levels, and for estrogens in enhancing TRH-induced responses
AU McKenna, T. Joseph; Cunningham, Sean; Culliton, Marie; Daly, Leslie; Moore, Aideen; Magee, Fergal; Smyth, Peter P. A.
CS Dep. Endocrinol., St. Vincent's Hosp., Dublin, Ire.
SO Acta Endocrinol. (Copenhagen) (1984), 106(1), 15-20
CODEN: ACENA7; ISSN: 0001-5598
DT Journal
LA English
AB The possibility that elevated prolactin levels are involved in the pathogenesis of hyperandrogenemia in hirsute patients was studied. Basal prolactin levels in hirsute women, with or without menstrual disturbances, 201 milliunit (mU)/L and 192 mU/L resp., were significantly suppressed below levels in normal women, 289 mU/L. The prolactin response to TRH (max. increment or integrated response) was exaggerated in hirsute women with menstrual disturbances when compared to normal women, to hirsute women with normal menses, or to normal men. This abnormal response may have been due to elevated estrone levels present in patients with oligomenorrhea (318 compared to 191 in normal women and 161 pmol/L in hirsute women with normal menses). There were no abnormalities detected in the suppression of prolactin in response to L-dopa in any of these groups. These finding do not support a role for prolactin in the pathogenesis of hyperandrogenemia in hirsute patients. However, elevated androgen levels in women may bring about suppression of basal prolactin levels to values seen in normal men. In addn., elevated estrone levels may exaggerate the stimulatory effect of TRH on prolactin secretion.

L24 ANSWER 14 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1984:21184 HCAPLUS
DN 100:21184
TI **Androgen metabolism** by isolated hairs from women with idiopathic **hirsutism** is usually normal
AU Glickman, Sally P.; Rosenfield, Robert L.
CS Pritzker Sch. Med., Univ. Chicago, Chicago, IL, 60637, USA

SO J. Invest. Dermatol. (1984), 82(1), 62-6
CODEN: JIDEAE; ISSN: 0022-202X
DT Journal
LA English
AB The hypothesis that idiopathic hirsutism (IH) may be due to abnormality of androgen-responsive hair follicles was tested. Because androgen metab. within target cells is an important determinant of androgen action, the rates of formation and disposition of the major mediators of androgen action, testosterone (T) and dihydrotestosterone (DHT), were analyzed. In normal women, the pattern of **androgen metab.** by **growing hairs** favors T predominance over DHT and inactivation of both these 17.beta.-hydroxysteroids to 17-ketosteroids. This pattern results greatly from predominance of 17.beta.-hydroxysteroid dehydrogenation. In normal women's scalp hair, DHT disposition to 5.alpha.-androstanedione proceeded at the rate of 8.6%/.mu.g DNA/min, whereas DHT was formed from T at a rate of 0.14, and T was formed from androstenedione at a rate of 0.60, all significantly different from one another. Both the formation of 17-ketosteroids and the apparent 5.alpha.-reductase activity were exaggerated in the pubic hair of men; whether these differences are site-, sex-, or androgen-related, remains to be detd. Pubic hairs tended to metabolize androgens at a greater rate than did scalp hair. This was related to the significantly greater DNA content of plucked pubic hairs, a difference unrelated to sex or androgen levels. Women with IH had heterogeneous pubic hair abnormalities. Only 1 of the 4 IH patients studied had abnormal pubic hair follicle androgen metab., with the greatest abnormality being exaggerated rate of 17.beta.-hydroxysteroid inactivation to 17-ketosteroids. Two of the other 3 IH cases had increased DNA content of plucked pubic hairs, a different kind of exaggeration of normal, which suggests an abnormality of hair follicle growth unrelated to androgen sensitivity. The concept that IH is related to various distinct types of sexual hair abnormalities which reflect fundamental defects in the regulation of hair growth is suggested.

L24 ANSWER 15 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1983:503064 HCAPLUS
DN 99:103064
TI A comparison of androgen production and clearance in hirsute and obese women
AU Kirschner, Marvin A.; Samojlik, Eugeniusz; Silber, Danuta
CS Newark Beth Israel Med. Cent., New Jersey Med. Sch., Newark, NJ, USA
SO J. Steroid Biochem. (1983), 19(1B), 607-14
CODEN: JSTBBK; ISSN: 0022-4731
DT Journal; General Review
LA English
AB A review and discussion with 56 refs.

L24 ANSWER 16 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1983:464320 HCAPLUS
DN 99:64320
TI Androgen metabolism in human skin: importance of dihydrotestosterone formation in normal and abnormal target cells
AU Mauvais-Jarvis, Pierre; Kuttenn, Frederique; Mowszowicz, Irene
CS Dep. Reprod. Endocrinol., Fac. Med. Necker, Paris, 75015, Fr.
SO Androg. Women: Pathophysiol. Clin. Aspects, [Collect. Pap. Int. Symp.] (1983), Meeting Date 1981, 47-63. Editor(s): Molinatti, Gian Michele; Martini, Luciano; James, Vivian Hector Thomas. Publisher:

Raven, New York, N. Y.
CODEN: 49UJA6
DT Conference; General Review
LA English
AB A review with 69 refs. on **androgen** metab. by human skin and on dihydrotestosterone [521-18-6] formation and its **metab**. to androstanediols in various skin areas in normal adults and in subjects with disorders of sex development, i.e., male pseudohermaphroditism and idiopathic **hirsutism**.

L24 ANSWER 17 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1983:464319 HCAPLUS
DN 99:64319
TI Ovarian and adrenal secretion of androgens
AU Serio, M.; Mannelli, M.; Calabresi, E.; Orlando, C.; Giannotti, P.
CS Univ. Sassari, Sassari, Italy
SO Androg. Women: Pathophysiol. Clin. Aspects, [Collect. Pap. Int. Symp.] (1983), Meeting Date 1981, 15-24. Editor(s): Molinatti, Gian Michele; Martini, Luciano; James, Vivian Hector Thomas. Publisher: Raven, New York, N. Y.
CODEN: 49UJA6
DT Conference; General Review
LA English
AB A review with 24 refs. on adrenal and ovarian **androgen** secretion and on intraovarian **metab**. of .DELTA.4-**androgens** and its importance in **hirsutism**.

L24 ANSWER 18 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1981:528684 HCAPLUS
DN 95:128684
TI Simultaneous determination of 5.alpha.-reduced metabolites of testosterone in human plasma
AU Toscano, V.; Petrangeli, E.; Adamo, M. V.; Foli, S.; Caiola, S.; Sciarra, F.
CS Ist. Clin. Med. V, Univ. Rome, Rome, 00100, Italy
SO J. Steroid Biochem. (1981), 14(6), 574-8
CODEN: JSTBBK; ISSN: 0022-4731
DT Journal
LA English
AB A radioimmunoassay is proposed for the simultaneous detn. of testosterone (I), dihydrotestosterone (II), 3.alpha.,17.beta.-dihydroxy-5.alpha.-androstane (III), and 3.beta.,17.beta.-dihydroxy-5.alpha.-androstane (IV) in blood plasma by using celite microcolumn chromatog. and 2 different antiserums. The concns. of the 4 androgens in normal males and females were, resp., 610.33 and 30.4 for I, 47.8 and 16.8 for II, 28.7 and 10.8 for III, and 54.9 and 23.9 ng/dL for IV. Results obtained in orchidectomized patients and **hirsute** women suggested that the detn. of 5.alpha.-reduced **metabolites** in peripheral plasma may be a useful clin. parameter for the evaluation of peripheral **androgen metab**.

L24 ANSWER 19 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1981:189852 HCAPLUS
DN 94:189852
TI **Androgen** secretion and skin **metabolism** in **hirsutism**
AU Mauvais-Jarvis, P.; Kuttenn, F.; Mowszowicz, I.
CS Dep. Reprod. Endocrinol., Fac. Med. Necker-Enfants-Malades, Paris,

Fr.
SO Res. Steroids (1981), 9(Endocrinol. Cancer, Ovarian Funct. Dis.), 337-46
CODEN: RSTEBF; ISSN: 0370-7466
DT Journal
LA English
AB The steroid 5.alpha.-reductase activity in pubic skin homogenates was higher for polycystic ovary syndrome women than for normal women. Androgen prodn. seemed to be increased in all hirsute women tested since the plasma levels of testosterone and androstenedione were above normal. Testosterone was esp. high in the plasma of patients with ovarian or adrenal dysfunction and almost normal in idiopathic hirsutism. The only androgen always increased was androstenedione. Apparently, the urinary excretion rate of androstenediol is a better discriminant of hirsutism than the dihydrotestosterone level of plasma. The increased excretion rate of androstanediol in hirsute patients reflects increases in the amt. of androstenedione produced and its peripheral conversion.

L24 ANSWER 20 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1981:2757 HCAPLUS
DN 94:2757
TI **Androgen** production and skin **metabolism** in idiopathic **hirsutism**
AU Mauvais-Jarvis, P.; Kuttenn, F.; Mowszowicz, I.
CS Dep. Reproductive Endocrinol., Fac. Med. Necker, Paris, 75730/15, Fr.
SO Recent Results Pept. Horm. Androg. Steroid Res., Proc. Congr. Hung. Soc. Endocrinol. Metab., 9th (1979), 223-33. Editor(s): Laszlo, F. A. Publisher: Akad. Kiado, Budapest, Hung.
CODEN: 44QOAY
DT Conference
LA English
AB Plasma androstenedione and testosterone levels of women with idiopathic hirsutism were above those for normal women but below those for cases of ovarian and adrenal virilism. The plasma level of dihydrotestosterone of women with idiopathic hirsutism was higher than for normal women but it did not differ from the level for women with ovarian or adrenal virilism. Urinary androstanediol was above normal in idiopathic hirsutism but women with polycystic ovaries had a higher level. Skin testosterone 5.alpha.-reductase activity was above normal in idiopathic hirsutism and this activity was comparable to that for normal men but higher than in adrenal virilism.

L24 ANSWER 21 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1981:2721 HCAPLUS
DN 94:2721
TI Metabolism of androgen steroids in human skin in patients with various endocrine disorders
AU Faredin, I.; Toth, I.
CS 1st Dep. Med., Univ. Med. Sch., Szeged, Hung.
SO Recent Results Pept. Horm. Androg. Steroid Res., Proc. Congr. Hung. Soc. Endocrinol. Metab., 9th (1979), 197-207. Editor(s): Laszlo, F. A. Publisher: Akad. Kiado, Budapest, Hung.
CODEN: 44QOAY
DT Conference
LA English
AB Two patients (19 and 46 yr old) with familial complete testicular

feminization were studied. Pubic skin of the younger patient formed testosterone (I) and 4-androstene-3,17-dione (II) from dehydroepiandrosterone (III) with high conversion. For the other patient these were normal. In both patients there was a subnormal conversion of I to III. The .DELTA.4-5.alpha.-reductase activity of skin and water-sol. C19-steroid sulfate of sweat were both subnormal for both patients. In a study on 2 patients (16 and 17 yr old) with idiopathic hirsutism I and II were formed in high yield from III by suprapubic skin of the 17 yr old. The other patient addnl. formed 5-androstene-3.beta.,17.beta.-diol. The skin of both patients synthesized III from II in above-normal yield. The skin of the 17 yr old patient metabolized I normally, but the skin of the other patient formed II in supranormal amts.

L24 ANSWER 22 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1979:472809 HCAPLUS
DN 91:72809
TI The role of the adrenal cortex in hirsutism
AU Abraham, Guy E.; Manlimos, Fredesminda S.
CS Sch. Med., Univ. California, Torrance, CA, 90509, USA
SO Proc. Serono Symp. (1978), 18(Endocr. Funct. Hum. Adrenal Cortex), 325-49
CODEN: PSSYDG; ISSN: 0308-5503
DT Journal
LA English
AB In 97 women with hirsutism, plasma cortisol, desoxycortisol, dehydroepiandrosterone sulfate, testosterone, dihydrotestosterone, and 17.alpha.-progesterone were measured before and after suppression of ACTH secretion by dexamethasone. Seven patients had normal plasma androgen concns. both before and after dexamethasone. Of the other 90 patients with hyperandrogenism, the adrenal gland was the source of the hyperandrogenism in 49 since dexamethasone normalized their plasma androgen values, 21 had an ovarian source since dexamethasone failed to normalize their plasma androgen values, and 20 had a mixed adrenal and ovarian source since their plasma androgen values were partially suppressed but remained elevated. Forty-six of the 90 patients had mild or moderate 11- and(or) 21-hydroxylase deficiency since the ratios of plasma desoxycortisol/cortisol and 17.alpha.-hydroxyprogesterone/cortisol were increased, resp. Two patients (not in the above group) with ovarian neoplasms had serum testosterone concns. >3 ng/mL and 3 patients with adrenal adenomas had serum dehydroepiandrosterone sulfate concns. >9000. All of the 90 hirsute patients had testosterone and dehydroepiandrosterone sulfate values below these values. Patients with ovarian hyperandrogenism had increased plasma LH levels. Plasma prolactin levels were normal in adrenal hyperandrogenism. Treatment of patients with mixed hyperandrogenism with dexamethasone for several months decreased both adrenal and ovarian steroids, indicating that elevated adrenal steroids may interfere with ovarian steroidogenesis.

L24 ANSWER 23 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1979:149182 HCAPLUS
DN 90:149182
TI Metabolic clearance rate and interconversion of androgens and the influence of the free androgen fraction
AU Vermeulen, Alex; Ando, Sebastiano
CS Sect. Endocrinol. Metab. Dis., Acad. Hosp., Ghent, Belg.
SO J. Clin. Endocrinol. Metab. (1979), 48(2), 320-6

CODEN: JCEMAZ; ISSN: 0021-972X
DT Journal
LA English
AB Using the continuous infusion technique, the conversion ratios (CR) of testosterone (T) to androstenedione (A) and dihydrotestosterone (DHT) and of A to T and DHT were detd. in normal males (aged 31-72 yr), normal postmenopausal women, and amenorrheic women with idiopathic hirsutism; in addnl. males, these studies were performed during infusion of cold T to increase plasma T to suprahysiol. levels. It was obsd. that in addn. to the metabolic clearance rate of T and DHT, the blood conversion ratios (CRBB) of T into A and to a lesser extent of T into DHT were also significantly correlated with either the free or the nontestosterone-estradiol-binding globulin-bound T fraction but not with total plasma T. In postmenopausal women, plasma A was by far the most important precursor of plasma DHT; the CRBB for A conversion to DHT was significantly higher than for T conversion to DHT. The total plasma A, but only nonspecifically bound T, might freely gain access into the cells where these conversions occur, and plasma A might be an important parameter of androgenicity. Less than 50% of plasma DHT could accounted for by peripheral conversion of either A or T. Whereas in males this may be explained by direct DHT secretion, in (postmenopausal) women, conversion of other precursors to plasma DHT should be considered.

L24 ANSWER 24 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1978:561029 HCAPLUS
DN 89:161029
TI Diagnostic approach to the hirsute patient
AU Genazzani, A. R.; Pecciarini-Snickars, L.; Franchi, F.; De Leo, V.; Picciolini, E.; Tarascio, P.
CS Dep. Obstet. Gynecol., Univ. Siena, Siena, Italy
SO Horm. Res. (1978), 9(6), 375-89
CODEN: HRMRA3; ISSN: 0301-0163
DT Journal; General Review
LA English
AB A review with 42 refs. of **androgen metab.** by females with emphasis on a diagnostic approach to the **hirsute** patient.

L24 ANSWER 25 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1978:473695 HCAPLUS
DN 89:73695
TI Physiopathogenesis of functional hypertrichosis. I. Particularities of androgen metabolism in functional hypertrichosis and overall physiopathogenesis
AU Buvat, J.; Buvat-Herbaut, M.
CS Lille, Fr.
SO Lille Med. (1978), 23(4), 252-8
CODEN: LIMEAD; ISSN: 0024-3507
DT Journal; General Review
LA French
AB A review with 35 refs.

L24 ANSWER 26 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1978:167745 HCAPLUS
DN 88:167745
TI Normal and abnormal androgen metabolism
AU Givens, James R.

CS Univ. Tennessee Coll. Med., Memphis, Tenn., USA
SO Clin. Obstet. Gynecol. (1978), 21(1), 115-23
CODEN: COGYAK; ISSN: 0009-9201
DT Journal; General Review
LA English
AB A review with 20 refs. with emphasis on **androgen metab.** in normal and **hirsute** women and in the fetus and neonate is presented.

L24 ANSWER 27 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1978:20192 HCAPLUS
DN 88:20192
TI **Androgen** production and skin **metabolism** in **hirsutism**
AU Kuttenn, Frederique; Mowszowicz, Irene; Schaison, Gilbert; Mauvais-Jarvis, Pierre
CS Dep. Med. Biochem., Fac. Med., Paris, Fr.
SO J. Endocrinol. (1977), 75(1), 83-91
CODEN: JOENAK
DT Journal
LA English
AB The plasma levels of testosterone (I), dihydrotestosterone, and androstenedione (II) and the urinary level of androstanediol (III) in hirsute women were all above control levels, esp. plasma II and urinary III. This was particularly marked in patients with ovarian hirsutism. Conversion of 3H-labeled I to 5.alpha.-reduced metabolites by skin homogenates was higher in hirsute women than in normal women, but was similar to that in control men. The highest conversion was obsd. in patients with idiopathic hirsutism. II was the major androgen secreted in hirsutism and increased activity of I 5.alpha.-reductase may result in exaggerated utilization of II in sexual skin. The high excretion rate of III in idiopathic hirsutism may be a result of it being an end product of I metab.

L24 ANSWER 28 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1977:403544 HCAPLUS
DN 87:3544
TI **Androgen metabolism** in the skin of **hirsute** women
AU Oake, R. J.; Thomas, J. P.
CS Dep. Med., Welsh Natl. Sch. Med., Cardiff, Wales
SO Proc. Serono Symp. (1976), 7(Endocr. Funct. Hum. Ovary), 495-507
CODEN: PSSYDG
DT Journal; General Review
LA English
AB A review with 17 refs.

L24 ANSWER 29 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1977:403387 HCAPLUS
DN 87:3387
TI Androgenic hormones in hirsutism
AU Giusti, G.; Roncoli, E.; Forti, G.; Cattaneo, S.; Fiorelli, G.; Pazzagli, M.; Serio, M.
CS Endocrinol. Unit, Univ. Florence, Florence, Italy
SO Proc. Serono Symp. (1976), 7(Endocr. Funct. Hum. Ovary), 437-42
CODEN: PSSYDG
DT Journal; General Review
LA English
AB A review with 18 refs. on androgen secretion by the adrenals and

ovaries, plasma binding and metab. of androgens, and skin metab. of androgens.

L24 ANSWER 30 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1977:135913 HCAPLUS
DN 86:135913
TI Diagnostic evaluation of hirsutism in women
AU Farber, Martin; Millan, Victor G.; Turksoy, R. Nuran; Mitchell, George W., Jr.
CS Sch. Med., Tufts Univ., Boston, Mass., USA
SO Clin. Obstet. Gynecol. (1977), 20(1), 1-9
CODEN: COGYAK
DT Journal
LA English
AB The **metab**. of **androgens** and diagnostic methods to evaluate **hirsutism** in women (urinary **androgen** detns., plasma **androgen** detn., adrenal and ovarian stimulation and suppression tests, and ovarian and adrenal venous catheterization studies) are described. In addn., case histories are presented that suggest that bilateral selective ovarian and adrenal venous catheterization may be used most advantageously to det. the major source(s) of androgen secretion in hirsute women. The suppressibility of plasma testosterone after dexamethasone administration is apparently effective therapeutically, with the use of estrogen-progesterogen pills if dexamethasone is not effective. Catheterization data pinpoint the ovaries as a significant source of testosterone secretion.

L24 ANSWER 31 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1977:69428 HCAPLUS
DN 86:69428
TI **Androgens** and their **metabolites**. Current results in normal and **hirsute** women
AU Bercovici, J. P.
CS Serv. Endocrinol., Cent. Hosp. Univ. Brest, Brest, Fr.
SO Nouv. Presse Med. (1976), 5(41), 2797-801
CODEN: NPMDAD
DT Journal; General Review
LA French
AB A review with 15 refs. of the secretion, prodn., and metab. of androgens (testosterone and .DELTA.-4-androstenedione) in relation to virilization in women.

L24 ANSWER 32 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1976:38982 HCAPLUS
DN 84:38982
TI Testosterone **metabolism** in the skin. Review of its function in **androgenetic** alopecia, acne vulgaris, and idiopathic **hirsutism** including recent studies with antiandrogens
AU Price, Vera H.
CS Sch. Med., Univ. California, San Francisco, Calif., USA
SO Arch. Dermatol. (1975), 111(11), 1496-502
CODEN: ARDEAC
DT Journal; General Review
LA English
GI For diagram(s), see printed CA Issue.
AB A review with 68 refs. on testosterone (I) [58-22-0] metab. in the skin. Antiandrogen treatment and the role of 5.alpha.-

dihydrotestosterone [521-18-6] in the pathophysiol. of androgenetic alopecia, acne vulgaria, and idiopathic hirsutism is also discussed.

L24 ANSWER 33 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1972:97491 HCAPLUS
DN 76:97491
TI Adrenal and ovarian contributions to elevated free plasma androgen levels in hirsute women
AU Rosenfield, Robert L.; Ehrlich, Edward N.; Cleary, Robert E.
CS Pritzker Sch. Med., Univ. Chicago, Chicago, Ill., USA
SO J. Clin. Endocrinol. Metab. (1972), 34(1), 92-8
CODEN: JCEMAZ
DT Journal
LA English
AB Androgen production was increased in 6 nonhirsute normal females, 9 hirsute women with amenorrhea or oligomenorrhea (AH), and in 5 hirsute subjects with normal menstrual histories ("eumenorrheic hirsutism," EH) as detd. by measuring indexes for free (unbound) androgen levels and several intermediates in androgen biosynthesis. Dexamethasone (I) was given to suppress ACTH secretion and hence, ACTH-dependent androgen production by the adrenals. Human chorionic gonadotropin (HCG) was used subsequently during continued I administration to stimulate ovarian androgen production. The free plasma androgen levels were significantly higher in AH women than in either normal or EH subjects following the administration of I. The failure of I to suppress plasma free androgens to normal levels in AH women was probably due to overproduction of ovarian androgens. HCG administration reproduced the androgenic abnormality in this group. Apparently ACTH-dependent androgen production was normal in AH women because after I administration the abs. decrease in total and free androgen levels in these subjects was similar to that obsd. in normal and EH women. The data suggest that normal adrenal androgen production was probably superimposed on overproduction of androgen by the ovary. Adrenal androgen production may not be regulated in a neg. feedback fashion by the level of plasma androgens. The secretion of adrenal androgens is probably detd. by factors regulating ACTH secretion. Elevated levels of free androgens in the plasma do not appear to interfere with ovulation in EH women, and it is suggested that androgens have a relatively weak effect on the female gonadotropin releasing mechanism.

L24 ANSWER 34 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1971:138130 HCAPLUS
DN 74:138130
TI Dynamics of **androgen metabolism** in women with **hirsutism**
AU Bardin, C. Wayne; Mahoudeau, J. A.
CS Endocrinol. Branch, Natl. Cancer Inst., Bethesda, Md., USA
SO Ann. Clin. Res. (1970), 2(4), 251-62
CODEN: ACLRBL
DT Journal
LA English
AB In normal women, testosterone and several prehormones are secreted into the blood by the adrenals and ovaries. The adrenals can secrete a significant but variable fraction of blood testosterone in virilized women. A small amt. (2.5-20%) of the blood testosterone in normal women could be secreted by the ovaries. In a variety of pathol. conditions such as polycystic ovaries, tumors, and hyperthecosis, they accounted for a much larger fraction of

testosterone production. Androstenedione is the most important prehormone for plasma androgen, accounting for .apprx.50% of the testosterone in normal women. In virilized patients it accounted for only about 25%. Dehydroepiandrosterone (DHA) -accounts for .apprx.20% in normal women. Pre-hormone conversion to testosterone occurs in the liver and peripheral tissue. Thirty-five of 37 hirsute women with idiopathic hirsutism and polycystic ovaries had increased testosterone production rates but 14 of these had plasma testosterone levels in the normal range. The androgens other than testosterone which are likely to be important in hirsutism are dehydrotestosterone, the androstanediols, and androstenediol.

L24 ANSWER 35 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1969:85635 HCAPLUS
DN 70:85635
TI Testosterone and androstenedione production and interconversion rates in hirsute women
AU Bardin, C. Wayne; Lipsett, Mortimer B.
CS Endocrinol. Br., Nat. Cancer Inst., Bethesda, Md., USA
SO Testosterone, Proc. Workshop Conf. (1968), Meeting Date 1967, 226-31. Editor(s): Tamm, Juergen. Publisher: Georg Thieme Verlag, Stuttgart, Ger.
CODEN: 20VDAC
DT Conference
LA English
AB In patients with polycystic ovaries and hirsutism or with idiopathic hirsutism, there was consistently increased testosterone (I) in the blood. Androstenedione (II) production rates were generally increased in these women. In normal women, 49% of the plasma I resulted from conversion of plasma II. In the 2 groups of hirsute women, only 26% of the plasma I was so derived; and much of the excess I was probably secreted by either the ovary or the adrenal cortex.

L24 ANSWER 36 OF 36 HCAPLUS COPYRIGHT 1998 ACS
AN 1967:450708 HCAPLUS
DN 67:50708
TI In vitro metabolism of androgens in whole human blood
AU Blaquier, Jorge; Forchielli, Enrico; Dorfman, Ralph I.
CS Stanford Ind. Park, Palo Alto, Calif., USA
SO Acta Endocrinol. (Copenhagen) (1967), 55(4), 697-704
CODEN: ACENA7
DT Journal
LA English
AB Radioactive dehydroepiandrosterone, testosterone, androstenedione, 5-androstene-3.beta.,17.beta.-diol, and 4-androstene-3.beta.,17.beta.-diol were incubated with whole blood obtained from normal males and females and from subjects with idiopathic hirsutism. Results show that transformations and interconversions of androgens can take place in whole blood and of special interest is the transformation of the less to the more biol. active androgens. Implications of these changes in the possible role of blood in the control of endocrine homoeostasis are discussed.

```
=> d his

     (FILE 'HOME' ENTERED AT 11:13:32 ON 29 OCT 1998)

     FILE 'HCAPLUS, BIOSIS, MEDLINE, BIOBUSINESS, BIOTECHDS, EMBASE'
     ENTERED AT 11:13:58 ON 29 OCT 1998
L1          4139 S (ANDROGEN OR TESTESTERON?) AND (HAIR(3A)GROW? OR ALOPEC
L2            18 S L1 AND INACTIVE?
L3            13 S L2 AND (METABOL? OR CONVERT? OR CHANG?)
L4             0 S L3 NOT L2
L5             7 DUP REMOV L3 (6 DUPLICATES REMOVED)
L6             9 DUP REMOV L2 (9 DUPLICATES REMOVED)
```

=> d bib abs 1-9

L6 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 1998 ACS DUPLICATE 1
AN 1997:215720 HCAPLUS
DN 126:233099
TI 19-Nor-10-azasteroids: A Novel Class of Inhibitors for Human Steroid 5.alpha.-Reductases 1 and 2
AU Guarna, Antonio; Belle, Catherine; Machetti, Fabrizio; Occhiato, Ernesto G.; Payne, Andrew H.; Cassiani, Chiara; Comerci, Alessandra; Danza, Giovanna; De Bellis, Alessandra; Dini, Stefania; Marrucci, Alessandro; Serio, Mario
CS Dipartimento di Chimica Organica Ugo Schiff, Universita di Firenze, Florence, I-50121, Italy
SO J. Med. Chem. (1997), 40(7), 1112-1129
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CJACS
AB Steroid 5.alpha.-reductase is a system of two isoenzymes (5.alpha.R-1 and 5.alpha.R-2) which catalyzes the NADPH-dependent redn. of testosterone to dihydrotestosterone in many **androgen** sensitive tissues and which is related to several human endocrine diseases such as benign prostatic hyperplasia (BPH), prostatic cancer, acne, **alopecia**, pattern baldness in men and **hirsutism** in women. The discovery of new potent and selective 5.alpha.R inhibitors is thus of great interest for pharmaceutical treatment of these diseases. The synthesis of a novel class of inhibitors for human 5.alpha.R-1 and 5.alpha.R-2, having the 19-nor-10-azasteroid skeleton, is described. The inhibitory potency of the 19-nor-10-azasteroids was detd. in homogenates of human hypertrophic prostates toward 5.alpha.R-2 and in DU-145 human prostatic adenocarcinoma cells toward 5.alpha.R-1, in comparison with finasteride (IC50 = 3 nM for 5.alpha.R-2 and .apprx. 42 nM for 5.alpha.R-1), a drug which is currently used for BPH treatment. The inhibition potency was dependent on the type of substituent at position 17 and on the presence and position of the unsatn. in the A and C rings. .DELTA.9(11)-19-Nor-10-azaandrost-4-ene-3,17-dione (or 10-azaestra-4,9(11)-diene-3,17-dione) and 19-nor-10-azaandrost-4-ene-3,17-dione were weak inhibitors of 5.alpha.R-2 (IC50 = 4.6 and 4.4 .mu.M, resp.) but more potent inhibitors of 5.alpha.R-1 (IC50 = 263 and 299 nM, resp.), whereas 19-nor-10-aza-5.alpha.-androstane-3,17-dione was **inactive** for both the isoenzymes. The best result was achieved with the 9:1 mixt. of .DELTA.9(11)- and .DELTA.8(9)-17.beta.-(N-tert-butylcarbamoyl)-19-nor-10-aza-4-androsten-3-one, which was a good inhibitor of 5.alpha.R-1 and 5.alpha.R-2 (IC50 = 127 and 122 nM, resp.), with a potency very close to that of finasteride. The results of ab initio calcns. suggest that the inhibition potency of 19-nor-10-azasteroids could be directly related to the nucleophilicity of the carbonyl group in the 3-position.

L6 ANSWER 2 OF 9 BIOBUSINESS COPYRIGHT 1998 BIOSIS
AN 97:35974 BIOBUSINESS
DN 0893509
TI 19-Nor-10-azasteroids: A novel class of inhibitors for human steroid 5-alpha-reductases 1 and 2.

AU Guarna A; Belle C; Machetti F; Occhiato E G; Payne A H; Cassinai C; Comerci A; Danza G; Bellis A D; Dini S; Maurrucci A; Serio M
CS Dip. Chim. Organ., Univ. Firenze, Via Gino Capponi 9, I-50121 Firenze, Italy.
SO Journal of Medicinal Chemistry, (1997) Vol.40, No.7, p.1112-1129. ISSN: 0022-2623.
DT ARTICLE
FS NONUNIQUE
LA English
AB Steroid 5-alpha-reductase is a system of two isozymes (5-alpha-R-1 and 5-alpha-R-2) which catalyzes the NADPH-dependent reduction of testosterone to dihydrotestosterone in many **androgen** sensitive tissues and which is related to several human endocrine diseases such as benign prostatic hyperplasia (BPH), prostatic cancer, acne, **alopecia**, pattern baldness in men and **hirsutism** in women. The discovery of new potent and selective 5-alpha-R inhibitors is thus of great interest for pharmaceutical treatment of these diseases. The synthesis of a novel class of inhibitors for human 5-alpha-R-1 and 5-alpha-R-2, having the 19-nor-10-azasteroid skeleton, is described. The inhibitory potency of the 19-nor-10-azasteroids was determined in homogenates of human hypertrophic prostates toward 5-alpha-R-2 and in DU-145 human prostatic adenocarcinoma cells toward 5-alpha-R-1, in comparison with finasteride (IC-50 = 3 nM for 5-alpha-R-2 and apprx 42 nM for 5-alpha-R-1), a drug which is currently used for BPH treatment. The inhibition potency was dependent on the type of substituent at position 17 and on the presence and position of the unsaturation in the A and C rings. DELTA-9(11)-19-Nor-10-azaandrost-4-ene-3,17-dione (or 10-azaestra-4,9(11)-diene-3,17-dione) (4a) and 19-nor-10-azaandrost-4-ene-3,17-dione (5) were weak inhibitors of 5-alpha-R-2 (IC-50 = 4.6 and 4.4 mu-M, respectively) but more potent inhibitors of 5-alpha-LR-1 (IC-50 = 263 and 299 nM, respectively), whereas 19-nor-10-aza-5-alpha-androstane-3,17-dione (7) was **inactive** for both the isoenzymes. The best result was achieved with the 9:1 mixture of DELTA-9(11)- and DELTA-8(9)-17-beta-(N-tertbutylcarbamoyl)-19-nor-10-aza-4-androsten-3-one (10ab) which was a good inhibitor of 5-alpha-R-1 and 5-alpha-R-2 (IC-50 = 127 and 122 nM, respectively), with a potency very close to that of finasteride. The results of ab initio calculations suggest that the inhibition potency of 19-nor-10-azasteroids could be directly related to the nucleophilicity of the carbonyl group in the 3-position.

L6 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 1998 ACS
AN 1995:423802 HCAPLUS
DN 123:102007
TI Relationship between structure and activity of 5.alpha.-reductase inhibitors
AU Guarna, A.; Marrucci, A.; Danza, G.; Serio, M.
CS Department of Organic Chemistry "Ugo Schiff", Firenze, I-50121, Italy
SO Int. Congr. Ser. (1994), 1064(Sex Hormones and Antihormones in Endocrine Dependent Pathology), 93-108
CODEN: EXMDA4; ISSN: 0531-5131
DT Journal
LA English
AB The enzyme steroid 5.alpha.-reductase (E.C.1.3.99.5) (5.alpha.-R) is a system of two NADPH-dependent isoenzymes which catalyzes the conversion of testosterone (T) to dihydrotestosterone (DHT) in many

androgen-sensitive cells. The prodn. of DHT is related to several human endocrine diseases such as benign prostatic hyperplasia (BPH), prostatic cancer, baldness, acne, **alopecia** in men and **hirsutism** in women. Thus, the blockade of the DHT formation without deprivation of T, by using selective 5.alpha.-R inhibitors, is an important target in pharmaceutical and medical research. A mol. modeling study has been developed to establish the indispensable mol. features to inhibit the human prostatic enzyme 5.alpha.-R. The active site model was obtained using the "active analog approach", by taking the differences between the combined vols. of a set of **inactive** mols. and the combined vols. of a set of active mols. The resulting three-dimensional area represents a part of the space occupied by the enzyme. This approach is useful to predict the inhibitory activity of steroidal compds. towards 5.alpha.-R because the values of intersection with the cavity model are inversely correlated with the inhibitory potency of the compds. Therefore chem. syntheses can be directed towards the compds. which showed a good structure-activity relation.

L6 ANSWER 4 OF 9 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 2
AN 87:488061 BIOSIS
DN BA84:122704
TI CLINICAL AND HORMONAL EFFECTS OF CHRONIC GONADOTROPIN-RELEASING HORMONE AGONIST TREATMENT IN POLYCYSTIC OVARIAN DISEASE.
AU STEINGOLD K; DE ZIEGLER D; CEDARS M; MELDRUM D R; LU J K H; JUDD H L; CHANG R J
CS DEP. OBSTET. GYNECOL., UNIV. CALIF. SCH. MED., 22-177 CHS, LOS ANGELES, CA 90024.
SO J CLIN ENDOCRINOL METAB 65 (4). 1987. 773-778. CODEN: JCEMAZ ISSN: 0021-972X
LA English
AB Previously, we reported that short term administration of a highly potent GnRH agonist (GnRHa) for 1 month to patients with polycystic ovarian disease (PCO) resulted in complete suppression of ovarian steroidogenesis without measurable effects on adrenal steroid production. This new study was designed to evaluate the effects of long term GnRHa administration in PCO patients with respect to their hormone secretion patterns and clinical responses. Eight PCO patients and 10 ovulatory women with endometriosis were treated daily with sc injections of [D-His6-(imBzl), Pro9-NEt]GnRH (GnRHa; 100 .mu.g) for 6 months. Their results were compared to hormone values in 8 women who had undergone bilateral oophorectomies. In response to GnRHa, PCO and ovulatory women had rises of serum LH at 1 month, after which it gradually declined to baseline. In both groups FSH secretion was suppressed throughout treatment. Serum estradiol, estrone, progerterone, 17-hydroxyprogesterone, androstenedione, and testosterone levels markedly decreased to values found in oophorectomized women by 1 month and remained low thereafter. In contrast, serum pregnenolone and 17-hydroxypregnenolone were partially suppressed, and dehydroepiandrosterone, dehydroepiandrosterone sulfate, and cortisol levels did not change. Clinically, hyperplastic endometrial histology in three PCO patients reverted to an **inactive** pattern, and proliferative endometrium in two other PCO patients became **inactive** in one and did not change in the other. Regression of proliferative endometrial histology occurred in all ovulatory women. Vaginal bleeding occurred in all women studied during the first month of GnRHa administration, after which all but one PCO patient became

amenorrheic. Hot flashes were noted by all ovulatory women and by four of eight PCO patients. All PCO patients noted subjective reduction of skin oiliness, and five had decreased **hair growth**. We conclude that in premenopausal women: (1) chronic GnRHa administration results in apparently complete persistent suppression of ovarian steroid secretion; (2) adrenal steroid secretion is not influenced directly or indirectly; and (3) its use may be helpful in the treatment of endometrial hyperplasia and ovarian **androgen** excess in women with PCO.

L6 ANSWER 5 OF 9 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 3
AN 81:238402 BIOSIS
DN BA72:23386
TI **ANDROGEN** METABOLISM IN HUMAN SKIN.
AU KUTTENN F; MAUVAIS-JARVIS P
CS SERVICE D'ENDOCRINOL. ET DE GYNECOL. MED., HOPITAL NECKER, 149 RUE DE SEVRES, 75730 PARIS CEDEX 15, FRANCE.
SO INT J COSMET SCI 3 (1). 1981. 9-22. CODEN: IJCMDW ISSN: 0142-5463
LA French
AB In human beings, **androgen** metabolism is important in mediating the action of male hormones upon target structures of the skin. Human skin is capable of transforming **inactive** steroids supplied through the blood, such as androstenedione and dehydroisoandrosterone, into the active **androgen** testosterone. Human skin is able to reduce testosterone to 5.alpha.-dihydrotestosterone, an essential prerequisite, during embryogenesis, for the male differentiation of target structures derived from urogenital sinus. At puberty, **hair growth** in sexual areas of skin also requires the transformation of testosterone to dihydrotestosterone. Regulation of 5.alpha.-reductase activity varies according to the anatomical site of the enzyme. In fetuses, 5.alpha.-reductase activity present in tissues derived from the urogenital tract does not seem to be **androgen**-dependent, since it is acquired before the onset of testosterone secretion by fetal testis. The enzyme that mediates development of certain secondary sex characteristics, such as pilosebaceous gland activity in sexual areas, is clearly **androgen**-dependent, since it is absent before puberty and in persons with hypogonadism. The differences in the control of the 5.alpha.-reductase activity mediating the appearance of either primary or secondary sex characteristics are important and may explain the differences in 5.alpha.-reductase activity observed in adult skin of both sexes derived from different sexual areas. The knowledge of **androgen** relation to the skin is necessary to understand the action of the anti-**androgens**, particularly the compounds which may be used by topical administration.

L6 ANSWER 6 OF 9 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.
AN 78369667 EMBASE
TI [Female **hirsutism**: physiopathology and practical conclusions].
A PROPOS DES HYPERTRICHOSES FEMININES PHYSIOPATHOLOGIE ET CONCLUSIONS PRATIQUES.
AU Blaizot O.
CS Serv. Clin. Gynecol., Hop. St-Andre, Bordeaux, France
SO BORDEAUX MED., (1978) 11/16 (1427-1440).
CODEN: BOMEBE
CY France
LA French

SL English
AB Human hairiness depends upon hereditary, exogenous and endocrine factors. **Androgens** are of major importance in determining the aspect and localization of hairs. In women the principal plasmatic **androgens** are **inactive** but there is no protective system against hyperandrogenia. On the contrary, the excess **androgens** will, by different processes, increase the specific peripheric metabolism of testosterone, particularly in hair follicles and sebaceous glands. Once the possibility of a static constitutional **hirsutism** has been eliminated, the clinician must question the patient and undertake a thorough physical examination and a minimum of complementary investigations, in order to determine the ovarian or adrenal origin of the hyperandrogenia (often without success). The treatment should aim at both the symptom and its cause. Whenever possible one should prescribe an etiological treatment, but, if not, the only possibility is a palliatory treatment most often by the use of an estrogen-gestagen combination. One must not forget the dramatic psychological effects of such a disorder.

L6 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 1998 ACS DUPLICATE 4
AN 1979:119194 HCAPLUS
DN 90:119194
TI Peripheral conversion and uptake of **androgens** in XXY-man with Klinefelter's syndrome
AU Sulcova, J.; Jirasek, J. E.; Neuwirth, J.; Raboch, J.; Starka, L.
CS Fac. Gen. Med., Charles Univ., Prague, Czech.
SO Endokrinologie (1978), 72(3), 304-10
CODEN: ENDKAC; ISSN: 0013-7251
DT Journal
LA English
AB The conversion of testosterone and the uptake of testosterone and 5.alpha.-dihydrotestosterone were investigated in pubic skin and pubic hair follicles of a XXY-man with inadequate pubic hair. The uptake of both **androgens** was demonstrated in the skin and in the hair follicles. Activity of steroid 5.alpha.-reductase was present in both tissues. The total conversion of testosterone was 2-3-fold higher in the patient than in controls. In the XXY-man, the major metabolites were 5.alpha.- and 5.beta.-androstanediols, whereas in the normal men 5.alpha.-dihydrotestosterone and 4-androstenedione were mainly formed from testosterone. An explanation of the inadequate **growth** of pubic **hair** in the patient seemed to be related to a conversion of testosterone to its relatively **inactive** metabolites.

L6 ANSWER 8 OF 9 MEDLINE
AN 75208881 MEDLINE
DN 75208881
TI Concentration of unconjugated adrenogenic hormones and their precursors in normal and polycystic ovaries.
AU Gyory G; Kiss C; Feher T; Poteczin E
SO ENDOKRINOLOGIE, (1975 Jan) 64 (2) 181-90.
Journal code: EHJ. ISSN: 0013-7251.
CY GERMANY, EAST: German Democratic Republic
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197512
AB Dehydroepiandrosterone, androstenedione, testosterone, pregnenolone

and progesterone concentration was determined by our sensitive gas-liquid chromatographic method in ovarian tissues obtained from surgery of patients without **hirsutism** and with Stein-Leventhal syndrome. The steroids, except testosterone, were detectable in all ovaries studied. Dehydroepiandrosterone and androstenedione, regarded as preandrogens, were present in an increased amount in almost all patients with polycycstic ovaries. Gas chromatographic evidence was obtained for the presence of testosterone in two of the cases. The delta4/3betaOH ratio reflecting 3beta-hydroxysteroid dehydrogenase activity was decreased only in same patients with the Stein-Leventhal syndrome suggesting that the impaired function of this enzyme is not an obligatory feature of polycystic ovaries. Concentration of pregnenolone and progesterone measured in a part of cases varied in a great range although the determination was caried out before luteal phase. Simultaneous determination of hormones in both ovarian tissues revealed an active and an **inactive** period of the gland in the given time, since a great difference of hormone concentration in bilateral ovarian tissues were observed. A comparison of hormone content in ovaries and the urinary excretion of metabolites showed poor correlation between the two parameters of hormone production.

L6 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 1998 ACS
AN 1967:515161 HCAPLUS
DN 67:115161
TI Endocrine studies in a patient with virilism, ovarian stromal hyperplasia, and endometrial carcinoma
AU Mahesh, Virendra B.; McDonough, Paul G.; Greenblatt, Robert B.
CS Med. Coll. of Georgia, Augusta, Ga., USA
SO Obstet. Gynecol. (N. Y.) (1967), 30(4), 584-90
CODEN: OBGNAS
DT Journal
LA English
AB A patient with marked **hirsutism**, **alopecia**, and menstrual irregularities was studied. Histol. studies after hysterectomy and bilateral salpingo-oophorectomy showed ovarian stromal hyperplasia and endometrial carcinoma in situ or marked adenomatous hyperplasia. Urinary steroid studies 4 years before the operation showed excessive ovarian **androgen** secretion. Later studies just before and after operation indicated that the ovarian stroma was relatively **inactive** in steroid secretion.

=> d 1-20 bib abs

L28 ANSWER 1 OF 20 HCAPLUS COPYRIGHT 1998 ACS
AN 1998:330979 HCAPLUS
DN 129:49092
TI Hair regrowth: therapeutic agents
AU Shapiro, Jerry; Price, Vera H.
CS Division of Dermatology, University of British Columbia Hair Research and Treatment Centre, University of British Columbia, Vancouver, BC, Can.
SO Dermatol. Clin. (1998), 16(2), 341-356
CODEN: DRMCDJ; ISSN: 0733-8635
PB W. B. Saunders Co.
DT Journal; General Review
LA English
AB A review with 115 refs. This article reviews the current state of the art for two of the most common forms of hair loss encountered in clin. practice, **androgenetic alopecia** and **alopecia** areata. Current strategies based on recent advances in the understanding of disordered **hair growth** are discussed. Specific agents reviewed include **androgen** receptor proteins and steroid-**metabolizing enzymes** (5 .alpha.-reductase and aromatase) for **androgenetic alopecia**, and immunomodulators (corticosteroids, PUVA and anthralin) and biol. response modifiers (minoxidil) for **alopecia** areata.

L28 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 1998 ACS
AN 1997:696670 HCAPLUS
DN 128:7304
TI Combination therapy for androgenic alopecia with antisense oligonucleotides and minoxidil
IN Hoke, Glenn D. Jr
PA Dyad Pharmaceutical Corporation, USA; Hoke, Glenn D. Jr.
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
PI WO 9738728 A1 19971023
DS W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG
AI WO 97-US6133 19970414
PRAI US 96-15488 19960415
DT Patent
LA English
AB Minoxidil has been shown to stimulate **hair growth** or inhibit the loss of hair in a no. of patients beginning to develop **androgenic alopecia**. The mechanism by which minoxidil (2,4-pyrimidinediamine, 6-(1-piperidinyl)-3-oxide) alters the **hair growth** cycle is uncertain, but is thought to act by increasing vascular circulation to the hair follicle. Inhibitors of steroid **metab.**, particularly those that inhibit the conversion of **testosterone** to dihydrotestosterone, have shown effects on hair cycles, including inhibition of hair loss. One class of **enzymes** targeted by

these inhibitors are the steroid 5-.alpha.-reductases. Minoxidil used in conjunction with effectors of steroid **metab.**, leads to enhanced **hair growth** and decreased rates of hair loss. This specification relates to the use of antisense oligonucleotides targeting 5-.alpha.-reductases used in conjunction with other **hair growth** enhancers and/or hair loss inhibitors.

L28 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 1998 ACS
AN 1997:196639 HCAPLUS
DN 126:259934
TI Association of the steroid synthesis gene CYP11a with polycystic ovary syndrome and hyperandrogenism
AU Gharani, Neda; Waterworth, Dawn M.; Batty, Sari; White, Davinia; Gilling-Smith, Carole; Conway, Gerard S.; McCarthy, Mark; Franks, Stephen; Wiilliamson, Robert
CS Dep. Mol. Genet., Imperial Coll. Sch. Med., London, W2 1PG, UK
SO Hum. Mol. Genet. (1997), 6(3), 397-402
CODEN: HMGEE5; ISSN: 0964-6906
PB Oxford University Press
DT Journal
LA English
AB Biochem. data implicate an underlying disorder of **androgen** biosynthesis and/or **metab.** in the etiol. of polycystic ovary syndrome (PCOS). The authors have examd. the segregation of the genes coding for two key **enzymes** in the synthesis and **metab.** of **androgens**, cholesterol side chain cleavage (CYP11a) and aromatase (CYP19), with PCOS in 20 multiply-affected families. All analyses excluded CYP19 co-segregation with PCOS, demonstrating that this locus is not a major determinant of risk for the syndrome. However, the results provide evidence for linkage to the CYP11a locus (NPL score = 3.03). Parametric anal. using a dominant model suggests genetic heterogeneity, generating a max. HLOD score of 2.7 (.alpha. = 0.63). An assocn. study of 97 consecutively identified Europids with PCOS and matched controls demonstrates significant allelic assocn. of a CYP11a 5' UTR pentanucleotide repeat polymorphism with **hirsute** PCOS subjects. A strong assocn. was also found between alleles of this polymorphism and total serum **testosterone** levels in both affected and unaffected individuals. The authors' data demonstrate that variation in CYP11a may play an important role in the etiol. of hyperandrogenemia which is a common characteristic polycystic ovary syndrome.

L28 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 1998 ACS
AN 1996:438736 HCAPLUS
DN 125:110961
TI Messenger RNA expression of steroidogenesis **enzyme** subtypes in the human pilosebaceous unit
AU Courchay, Guy; Boyera, Nathalie; Bernard, Bruno A.; Mahe, Yann
CS Hair Biology Research Group, Centre de Recherche C. Zviak, Clichy, F-92583, Fr.
SO Skin Pharmacol. (1996), 9(3), 169-176
CODEN: SKPHEU; ISSN: 1011-0283
DT Journal
LA English
AB In order to define the resp. involvement of steroidogenesis **enzymes** subtypes in the control of hair follicle homeostasis, the authors evaluated, by semiquant. RT/PCR, the

expression levels of mRNAs coding for 17.beta.-hydroxysteroid dehydrogenase type 1 and type 2, 3.beta.-hydroxysteroid dehydrogenase, Cyt.P 450-aromatase, steroid 5.alpha.-reductase type 1 and type 2 and 11.beta.-hydroxysteroid dehydrogenase. These assays were performed for several components of the pilosebaceous unit (PSU); fresh plucked anagen hairs, sebaceous glands and primary culture of dermal papilla, as well as other tissues involved in an active steroid **metab**. (human testis, liver, placenta, prostate, ovary, uterus and adrenals) as controls. The authors found that plucked hair (i.e. mainly keratinocytes from the inner and outer root sheaths) expressed: (1) very high levels of 17.beta.-hydroxysteroid dehydrogenase type 2 corresponding to levels found in liver and placenta; (2) high levels of steroid 5-.alpha.-reductase type 1 corresponding to levels found in testis, liver and ovary, and moderate levels of 17.beta.-hydroxysteroid dehydrogenase type 1, which corresponded to the expression in testis, prostate and uterus. In contrast, Cyt.P 450-aromatase, 3.beta.-hydroxysteroid dehydrogenase and steroid 5.alpha.-reductase type 2 were poorly expressed in the pilosebaceous unit as compared with other tissues. Interestingly, expression patterns of these **enzymes** in primary cultures of dermal papilla were distinctive since 5.alpha.-reductase type 1 and 11.beta.-hydroxysteroid dehydrogenase were the only mRNA detected. Taken together, these results suggest that not only sebaceous gland but also outer root sheath keratinocytes may contribute, through the activity of the steroid 5.alpha.-reductase type 1, to the pathogenesis of **androgen**-dependent **alopecia**.

L28 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 1998 ACS
AN 1996:363770 HCAPLUS
DN 125:48057
TI 5.alpha.-Reductases and their inhibitors
AU Spera, G.; Lubrano, C.
CS Department Medical Physiopathology, University Rome "La Sapienza", Rome, Italy
SO Int. J. Immunopathol. Pharmacol. (1996), 9(1), 33-38
CODEN: IJIPE4; ISSN: 0394-6320
DT Journal; General Review
LA English
AB A review, with 7 refs. 5.alpha. Reductase is a key **enzyme** in **androgen metab**. Altered **enzyme** function and/or regulation is responsible for numerous human pathologies such as benign prostatic hyperplasia, acne, **hirsutism** and male pattern baldness. To block **androgen** action through inhibition of this **enzyme**, numerous compds. have been synthesized during the past two decades. Among them, 4-azasteroids and in particular finasteride have been extensively studied and used in the treatment of human diseases.

L28 ANSWER 6 OF 20 HCAPLUS COPYRIGHT 1998 ACS
AN 1996:300273 HCAPLUS
DN 124:339911
TI Comment: Predominant expression of 5.alpha.-reductase type 1 in pubic skin from normal subjects and hirsute patients
AU Mestayer, C.; Berthaut, I.; Portois, M.-C.; Kuttenn, Wright F.; Mowszowicz, I.; Mauvais-Jarvis, P.
CS Department of Endocrinology and Reproductive Medicine, Pitie-Salpetriere, Paris, Fr.
SO J. Clin. Endocrinol. Metab. (1996), 81(5), 1989-1993

CODEN: JCEMAZ; ISSN: 0021-972X
DT Journal
LA English
AB Dihydrotestosterone (DHT), the 5.alpha.-reduced **metabolite** of **testosterone**, is the active mol. triggering **androgen** action, and 5.alpha.-reductase (5.alpha.-R), the **enzyme** converting **testosterone** to DHT, is a key step in this mechanism. Skin, like prostate, is a DHT-dependent tissue. The authors' lab. demonstrated, many years ago, that 5.alpha.-R in external genitalia was not regulated by **androgens**, whereas it was **androgen** dependent in pubic skin. As two genes, 5.alpha.-R types 1 and 2, encoding for 5.alpha.-R **enzymes** have been recently cloned, the authors undertook the present study to det. whether the two **enzyme** the authors had postulated on the basis of regulation studies were coincident with the cloned isoforms. The expression of the two isoforms was studied in genital and pubic skin fibroblasts from normal men, normal women, and **hirsute** patients. The mRNA anal., using Northern blot and RT-PCR techniques, indicated that both 5.alpha.-R1 and -2 mRNAs are expressed in genital skin as well as in pubic skin fibroblasts. In contrast, studies using specific inhibitors of 5.alpha.-R1 (LY306089) and 5.alpha.-R2 (finasteride) showed that 5.alpha.-R2 **enzymic** activity is predominant in genital skin, whereas 5.alpha.-R1 is predominant in pubic skin of normal men, normal women, and **hirsute** patients. These data raise the question of the possible use of specific 5.alpha.-R1 inhibitors in the treatment of idiopathic **hirsutism**.

L28 ANSWER 7 OF 20 HCAPLUS COPYRIGHT 1998 ACS
AN 1996:239115 HCAPLUS
DN 124:338692
TI Immunolocalization of steroid 5.alpha.-reductase isoenzymes in human fetal skin
AU Eicheler, Wolfgang; Aumueller, Gerhard; Happle, Rudolf; Hoffmann, Rolf
CS Department Dermatology, Philipp University, Marburg, D-35033, Germany
SO Eur. J. Dermatol. (1996), 6(2), 132-4
CODEN: EJDEE4; ISSN: 1167-1122
DT Journal
LA English
AB The action of **androgens** is modulated by a no. of **metabolizing enzymes**. The key **enzymes** in activating **testosterone** in **androgen**-dependent tissues is steroid 5.alpha.-reductase which is present in two isoforms with different biochem. features and possibly different physiol. roles. The main functions of the skin, such as **hair growth** and secretory activity of sebaceous glands seem to be affected by steroid 5.alpha.-reductase activity. Therefore, specific inhibition of 5.alpha.-reductase has been regarded as a possible therapeutic concept in **androgenetic alopecia**, **hirsutism**, and acne. Despite of the potential importance of the **enzyme** in the pathogenesis of these conditions, little is known about the isoenzyme specific expression pattern of 5.alpha.-reductase during embryogenesis. Thus, specific polyclonal antisera were used to immunolocalize 5.alpha.-reductase isoenzymes in paraffin-embedded human fetal skin specimens between the 10th and 40th week of gestation. Isoenzyme 1 appeared first in the early epidermis. Nuclear staining was

detected in hair follicles, and sebaceous glands. It was present in most cell types of the dermal and epidermal compartment. Isoenzyme 2 was only immunolocalized in differentiated hair follicles and the epidermis after week 30 of gestation. Thus, it is concluded that isoenzyme 1, but not isoenzyme 2, may have a function in the developing skin.

L28 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 1998 ACS
AN 1995:653225 HCAPLUS
DN 123:77842
TI The **enzyme** and inhibitors of 4-ene-3-oxosteroid 5.alpha.-oxidoreductase
AU Li, Xun; Chen, Cailin; Singh, Shankar; Labire, Fernand
CS Res. Center, C.H.U.L., Quebec City, PQ, Can.
SO Steroids (1995), 60(6), 430-41
CODEN: STEDAM; ISSN: 0039-128X
DT Journal; General Review
LA English
AB A review, with 111 refs. Since evidence of 5.alpha.-reductase activity in rabbit liver homogenate was discovered in 1954, the presence of this **enzyme** has been demonstrated in many other organs and tissues of mammalian species. 5.alpha.-Reductase selectively transform a 4-ene-3-oxosteroid (e.g., **testosterone**) irreversibly to the corresponding 5.alpha.-3-oxosteroid (e.g., 5.alpha.-dihydrotestosterone) in the presence of NADPH as an essential coenzyme at an optimal pH. However, excessive prodn. of 5.alpha.-dihydrotestosterone is the major cause of many **androgen**-related disorders, such as prostate cancer, benign prostatic hyperplasia, acne, female **hirsutism**, and male pattern baldness; therefore, inhibition of **androgenic** action by 5.alpha.-reductase inhibitors is a logical treatment. During the past two decades, research has focused on understanding the biol. functions and effects of 5.alpha.-reductase and its 5.alpha.-reduced **metabolites**: purifn. of the **enzyme**, substrates and **metabolites** ; characterization of their phys., chem., and biochem. properties; anal. of the amino acid sequence of the **enzyme**; synthesis of various classes of mols. as potential inhibitors; and examn. of the biol. activity of the inhibitors in vitro and/or in vivo. This review summarizes the biochem. studies on this **enzyme**, suggests the mechanisms of action of the **enzyme** or inhibitors, and discusses the chem. necessary for the prepn., structure-activity relationships, and in vitro and/or in vivo data obtained from the evaluation of nonsteroidal and steroidal compds. that have been tested as inhibitors of 5.alpha.-reductase. In particular, IC50 and Ki values for relevant compds. will be compared according to mol. class. This review could function as a comprehensive working ref. of what research has been accomplished so far and what problems remain to be solved in the future for those engaged in this interesting field.

L28 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 1998 ACS
AN 1995:416741 HCAPLUS
DN 122:184237
TI Clinical relevance of testosterone and dihydrotestosterone metabolism in women
AU Rittmaster, Roger S.
CS Camp Hill Medical Centre, Dalhousie University, Halifax, NS, Can.
SO Am. J. Med. (1995), 98(1A), 17S-21S

CODEN: AJMEAZ; ISSN: 0002-9343
DT Journal; General Review
LA English
AB A review, with 38 refs. **Androgens** are part of normal female physiol. When they are secreted in excess or when they cause unwanted symptoms such as **hirsutism** and male-pattern baldness, the term hyperandrogenism is used. In many hyperandrogenic women, there is no well-defined hormonal abnormality, but the women are simply on one end of a normal spectrum of **androgen** secretion and cutaneous **androgen** sensitivity. To be active in the skin, **testosterone** must be converted to dihydrotestosterone by the **enzyme** 5.alpha.-reductase. **Androgen** sensitivity is detd., in part, by 5.alpha.-reductase activity in the skin. This is a localized phenomenon, and there is no generalized increase in 5.alpha.-reductase activity in these women. Dihydrotestosterone can be converted to glucuronide and sulfate conjugates, including androstanediol glucuronide. These **androgen** conjugates have been proposed to be serum markers of cutaneous **androgen metab.**, but recent evidence indicates that they arise from adrenal precursors and are more likely to be markers of adrenal steroid prodn. and **metab.** Antiandrogens (**androgen** receptor blockers) are the best medical treatment of cutaneous hyperandrogenism. 5.alpha.-Reductase inhibitors have recently been approved for the treatment of benign prostatic hyperplasia, and research is currently underway to det. their effectiveness in treating **hirsutism** and male-pattern baldness.

L28 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 1998 ACS
AN 1994:601910 HCAPLUS
DN 121:201910
TI Hyperandrogenism, polycystic ovary syndrome, and hirsutism
AU Barnes, Randall B.
CS University Chicago, Chicago, IL, USA
SO Curr. Opin. Endocrinol. Diabetes (1994), 1ST ED., 200-5
CODEN: CENDES; ISSN: 1068-3097
DT Journal; General Review
LA English
AB A review with 46 refs. Disorders of androgen excess are among the most common reproductive endocrine abnormalities in women. Most cases of hyperandrogenism probably result from abnormal regulation of the androgen-forming **enzymes** in the ovary, adrenal, or both. This may be due to an intrinsic abnormality making the **enzyme** respond inappropriately to regulatory factors, or it may be secondary to excess or deficiency of endocrine factors such as LH or insulin or of paracrine or autocrine growth factors. Hyperandrogenism is assocd. with not only infertility and hirsutism but also insulin resistance, diabetes, and heart disease. Thus, its proper diagnosis and management is essential to the maintenance of good health. This review examines the sources, pathophysiol., long-term consequences, and therapy of androgen excess.

L28 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 1998 ACS
AN 1990:210694 HCAPLUS
DN 112:210694
TI Increase in plasma 5.alpha.-androstane-3.alpha.,17.beta.-diol glucuronide as a marker of peripheral androgen action in hirsutism: a side-effect induced by cyclosporine A
AU Vexiau, Patrick; Fiet, Jean; Boudou, Philippe; Villette, Jean Marie;

Feutren, Gilles; Hardy, Noah; Julien, Rene; Dreux, Claude; Bach, Jean Francois; Cathelineau, Gerard
CS Diabetol. Endocrinol. Dep., Hop. Saint-Louis, Paris, Fr.
SO J. Steroid Biochem. (1990), 35(1), 133-7
CODEN: JSTBBK; ISSN: 0022-4731
DT Journal
LA English
AB Dose-dependent hypertrichosis is a common dermatol. side-effect affecting the majority of patients treated with cyclosporine A (CSA). Previous studies have not demonstrated the influence of CSA on specific sex hormone levels. The aim of this study is to investigate whether CSA increases the activity of 5.alpha.-reductase, an **enzyme** which transforms **androgens** into dihydrotestosterone in peripheral tissues. The **metabolite** which best reflects this activity is 5.alpha.-androstane-3.alpha.,17.beta.-diol glucuronide (Adiol G). The study was carried out on insulin-dependent diabetes patients participating in the double-blind clin. trial. In addn. to Adiol G, **testosterone** (T), dehydroepiandrosterone sulfate (DHEA S), and sex hormone-binding globulin (SHBG) were assayed. Levels of Adiol G increased significantly in CSA-treated groups. There were not significant differences in this parameter before and during treatment in either the male or female placebo groups. During the treatment period, T, DHEA S, SHBG and the T/SHBG ratio did not significantly change with respect to their baseline values in any of the groups studied (comparison of means). Comparison showed a significant increase of DHEA S in CSA-treated groups. Thus, it is possible that CSA induces hypertrichosis or **hirsutism** by increasing 5.alpha.-reductase activity in peripheral tissues. Nevertheless, the role of increased DHEA S as a possible Adiol G precursor cannot be excluded.

L28 ANSWER 12 OF 20 HCAPLUS COPYRIGHT 1998 ACS
AN 1990:883 HCAPLUS
DN 112:883
TI Testosterone-estradiol binding globulin (TeBG) in hirsute patients treated with cyproterone acetate (CPA) and percutaneous estradiol
AU Vincens, M.; Mercier-Bodard, C.; Mowszowicz, I.; Kuttenn, F.; Mauvais-Jarvis, P.
CS Dep. Endrocrinol. Reprod. Med., Hop. Necker, Paris, 75743, Fr.
SO J. Steroid Biochem. (1989), 33(4A), 531-4
CODEN: JSTBBK; ISSN: 0022-4731
DT Journal
LA English
AB **Testosterone**-estradiol binding globin (TeBG) was studied in **hirsute** women, before and after 6-mo treatment with cyproterone acetate (CPA). CPA (50 mg) was administered orally on days 5-25 of the menstrual cycle and combined with 3 mg 17.beta.-estradiol (E2) administered percutaneously on days 16-25 of the cycle. TeBG was evaluated by a filter assay measuring [3H]dihydrotestosterone ([3H]DHT) binding capacity. Before treatment, the mean plasma TeBG level was 40 nM in **hirsute** patients, which is lower than TeBG value in normal women (60 nM) and intermediate between normal women and normal men (30 nM). After a 6-mo treatment, TeBG strikingly decreased to 22 nM, which is lower than pretreatment values and even less than TeBG level in normal men. Parallel TeBG assay by immunoelectrodiffusion in some of these **hirsute** patients provided similar results. With this treatment, plasma **testosterone** and .DELTA.4-

androstenedione, measured on 20-25 days of the cycle, decreased from 68 to 25 ng/dL, and 210 to 98 ng/dL, resp. Plasma estradiol decreased from 150 to 75 pg/mL. In contrast, urinary 3.alpha.-androstanediol glucuronide remained high; 112 and 123 .mu.g/24 h, resp., before and with CPA treatment. Three mechanisms have been proposed to explain TeBG decrease under CPA + E2 perutaneous treatment: (1) relative competition of CPA with labeled DHT in the TeBG-binding capacity assay, (2) relative hyupoestrogenism with this treatment, (3) a progestagen or even a partial agonistic **androgen** effect of CPA on TeBG synthesis in the liver. The 3rd mechanism appears to be predominant. In any case, TeBG decrease combined with the partial **enzymic** induction effect of CPA on the liver contributes to the increase in the **metabolic** clearance rate of T and the high urinary androstanediol levels previously reported with CPA treatment.

L28 ANSWER 13 OF 20 HCAPLUS COPYRIGHT 1998 ACS
AN 1987:531959 HCAPLUS
DN 107:131959
TI Is increased 5.alpha.-reductase activity a primary phenomenon in androgen-dependent skin disorders?
AU Dijkstra, Andre C.; Goos, C. M. A. A.; Cunliffe, William J.; Sultan, Charles; Vermorken, Alphons J. M.
CS Res. Unit. Cell. Differ. Transform., Univ. Nijmegen, Nijmegen, Neth.
SO J. Invest. Dermatol. (1987), 89(1), 87-92
CODEN: JIDEAE; ISSN: 0022-202X
DT Journal
LA English
AB **Testosterone metab**. was investigated in fractions of human skin, enriched in epidermis, dermis, sebaceous glands, and sweat glands, by histol. sectioning of skin punch biopsies, and the results were compared with 2 culturable skin cells, i.e., keratinocytes and fibroblasts. Since sebocytes could not be brought in culture, **metab**. was also investigated in the hamster flank model. In the epidermal tissue of the skin biopsies the predominant **metabolite** was androstenedione, formed by the **enzyme** 17.beta.-hydroxysteroid dehydrogenase. The same was true for cultured hair follicle keratinocytes. In the deeper skin layers the formation of androstenedione was markedly reduced, whereas the formation of 5.alpha.-reduced **metabolites** was highly increased, with a max. in the skin fractions contg. large sebaceous glands. Cultured shoulder skin fibroblasts showed a markedly different **testosterone metab**. compared with the sectioned skin biopsies, suggesting that dermal fibroblasts play a less important role in the overall skin **testosterone metab**. The present approach, allowing the comparison of **testosterone metab**. in different substructures of the same skin biopsy provides new evidence that the high 5.alpha.-reductase activity in the specific skin fractions must be mainly ascribed to the sebaceous glands. These results render a previous hypothesis, stating that the elevated level of 5.alpha.-reductase and subsequent formation of dihydrostestosterone in **androgenetic alopecia** and acne (usually accompanied by seborrhea) could therefore simply be the consequence of sebaceous gland enlargement, much stronger. This hypothesis is further evaluated by quant. correlation of sebaceous gland size with **enzyme** activity in the hamster flank model.

L28 ANSWER 14 OF 20 HCAPLUS COPYRIGHT 1998 ACS
AN 1984:488316 HCAPLUS
DN 101:88316
TI **Metabolism** and concentration of **androgenic** steroids in the abdominal skin of women with idiopathic **hirsutism**
AU Faredin, I.; Toth, I.
CS First Dep. Med., Univ. Med. Sch., Szeged, H-6701, Hung.
SO Acta Med. Hung. (1984), 41(1), 19-34
CODEN: AMEHDS
DT Journal
LA English
AB The abdominal skin of 3 women with idiopathic **hirsutism** contained increased concns. of **androgens** and increased **enzymic** capacity for **androgen** formation when compared with skin from healthy women. Blood levels of **androgens** were normal in 1 **hirsute** woman, indicating that her **hirsutism** was entirely attributable to the altered skin **metab**. Blood levels of 4-androstene-3,17-dione were above normal in the other 2 **hirsute** women, indicating that their **hirsutism** derived from a combination of altered skin **metab**. and high blood **androgen** levels.

L28 ANSWER 15 OF 20 HCAPLUS COPYRIGHT 1998 ACS
AN 1984:488315 HCAPLUS
DN 101:88315
TI **Metabolism** and concentration of **androgenic** steroids in abdominal skin of **hirsute** women with adrenogenital syndrome
AU Toth, I.; Faredin, I.
CS First Dep. Med., Univ. Med. Sch., Szeged, H-6701, Hung.
SO Acta Med. Hung. (1984), 41(1), 7-18
CODEN: AMEHDS
DT Journal
LA English
AB Two patients were studied. In one patient (with higher androgen overprodn.), more testosterone (Test.) than normal was formed from the precursors 3.beta.-hydroxy-5-androstene-17-one (DHA), 5-androstene-3.beta.,17.beta.-diol (.DELTA.5-diol), or 4-androstene-3,17-dione (.DELTA.4-dione), suggesting that the biosynthetic pathway involving 17.beta.-hydroxysteroid dehydrogenase and .DELTA.5-3.beta.-hydroxysteroid dehydrogenase was enhanced in the abdominal skin. Androgen formation was not increased in the less severely affected woman. The concns. of DHA, 3.alpha.-hydroxy-5.alpha.-androstane-17-one, .DELTA.4-dione, .DELTA.5-diol, Test., 17.beta.-hydroxy-5.alpha.-androstane-3-one, and C19-steroid sulfates were increased in the 2 patients as compared with healthy women. Apparently, hyperandrogenism exists in the skin of these patients.

L28 ANSWER 16 OF 20 HCAPLUS COPYRIGHT 1998 ACS
AN 1982:97972 HCAPLUS
DN 96:97972
TI Androgen metabolism in isolated human hair roots
AU Schweikert, H. U.; Wilson, J. D.
CS Med. Univ. Poliklin., Bonn, Fed. Rep. Ger.
SO Hair Res., [Proc. Int. Congr.], 1st (1981), Meeting Date 1979, 210-14. Editor(s): Orfanos, Constantin E.; Montagna, William,;

Stuettgen, Guenter. Publisher: Springer, Berlin, Fed. Rep. Ger.
CODEN: 47BGAO
DT Conference
LA English
AB To investigate the relation between **androgens** and **hair growth** the **metab.** of 3H-labeled **testosterone** [58-22-0] and 3H-labeled androstenedione [63-05-8] was assessed in isolated human hair roots. To quantitate **androgen metab.** in only a few hair roots, a micromethod was developed. Using this method, it was shown that both growing (anagen) and resting (telogen) hair roots originating from 10 different body sites contain 2 major **enzymic** systems namely 5.alpha.-reductase [9036-43-5] and 17.beta.-hydroxy steroid dehydrogenase [9015-81-0]. No significant relation was found, with either **testosterone** or androstenedione as a substrate, between the **androgen**-mediated growth of hair and the capacity to form 5.alpha.-**metabolites**. However, a significantly greater formation of 5.alpha.-androstanes was found in the frontal area of balding men than in the same area in nonbalding men. Since 5.alpha.-redn. is irreversible and the formation of 17-keto steroids is favored, androstanedione is the principal intracellular **androgen** in human hair roots. The complex **enzymic** machinery required to aromatize androstenedione to estrone [53-16-7] in human hair roots was shown.

L28 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 1998 ACS
AN 1977:40706 HCAPLUS
DN 86:40706
TI Testosterone metabolism in human scalp and beard hair follicles
AU Rizer, Ronald L.; Orentreich, Norman; Finch, Caleb E.
CS Orentreich Med. Group, New York, N. Y., USA
SO Hum. Hair Symp., [Pap.], 1st (1974), Meeting Date 1973, 346-62.
Editor(s): Brown, Algie C. Publisher: MEDCOM Press, New York, N. Y.
CODEN: 34QFAU
DT Conference
LA English
AB Human scalp and beard hair follicles actively **metabolized** **testosterone**-1,2-3H2 in vitro. The principal products formed by both hair follicle types after 2 h of incubation were androstanediol, androsterone, dihydrotestosterone, androstenedione, 5.beta.-androstanedione, 5.alpha.-androstanedione, and a water-insol. ester of dihydrotestosterone. Therefore, there are at least 6 potentially active **metabolic** pathways for **testosterone** catabolism in human scalp and beard hair follicles: (1) the redn. of a 3-one to 3.alpha.-ol; (2) the oxidn. of a 17.beta.-ol to 17-one; (3) the 5.alpha. satn. of a 4-5 double bond; (4) the 5.beta. satn. of a 4-5 double bond; (5) the esterification of a 17.beta.-ol; and (6) an unknown pathway, probably also an esterification. Under the conditions of the expt., **testosterone metab.**, **testosterone** uptake, and total **metabolite** formation were the same for scalp and beard follicles. Thus, the **enzymic** conversion of **testosterone** to a more powerful **androgen** may not be significant in the hormonal stimulation of **hair growth**. Similarly, this could also apply to the mol. basis of common baldness.

L28 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 1998 ACS
AN 1975:168418 HCAPLUS

DN 82:168418
TI Testosterone 5.alpha.-reduction in the skin of normal subjects and of patients with abnormal sex development
AU Kuttenn, Frederique; Mauvais-Jarvis, Pierre
CS Lab. Biol. Chem., Fac. Med. Pitie-Salpetriere, Paris, Fr.
SO Acta Endocrinol. (Copenhagen) (1975), 79(1), 164-76
CODEN: ACENA7
DT Journal
LA English
AB Human pubic skin was obtained from normal subjects and patients with abnormal sex differentiation. Skin samples (200 mg) supplemented with NADPH, were incubated for 1 hr with labeled **testosterone**. The conversion of **testosterone** to dihydrotestosterone, and 3.alpha.-, and 3.beta.-androstanediol was averaged 14.9% in 11 normal men and 3.6 in 8 normal women. In 4 children as in 4 young hypogonadotropic hypogonadal men, the conversion rate of **testosterone** to 5.alpha.-reduced **metabolites** was low (0.8 - 3.5%) and increased at puberty (13.5 - 19.2%). After administration of human chorionic gonadotropin for 3 months to 1 of the hypogonadal men, it reached 30.2%. Inversely, the formation of dihydrotestosterone and androstanediols from **testosterone** was suppressed in 2 men treated with large doses of estrogen. In 3 subjects with an incomplete form of testicular feminization syndrome, the conversion rate of **testosterone** to 5.alpha.-reduced **metabolites** was in the normal male range (6.4 - 18.3%), whereas it was low in 1 case of the complete form of the syndrome (1.5%). In 9 women with idiopathic **hirsutism**, the rate of 5.alpha.-reduced **metabolites** recovered from **testosterone** was close to that of normal men (13.5%). Evidently, in human subjects, there is a good correlation between **hair growth** in skin from a sexual area and the extent of **testosterone** 5.alpha.-redn. in this tissue. Such an **enzymic** activity might be induced by active **androgens**. Detn. of urinary 3.alpha.-androstanediol might prove of clin. interest in the evaluation of the **androgenic** status in human subjects.

L28 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 1998 ACS
AN 1969:54451 HCAPLUS
DN 70:54451
TI Advances in the field of androgenic steroidogenesis of the human skin
AU Julesz, Miklos
CS First Dep. Med., Univ. Med. Sch., Szeged, Hung.
SO Acta Med. (Budapest) (1968), 25(3-4), 273-85
CODEN: AMASA4
DT Journal
LA English
AB In human axillary hairs, a no. of 17-keto steroids and considerable amts. of dehydroepiandrosterone (I) and small amts. of androsterone were found. Most of the 17-keto steroids were present in the form of sulfate ester. Human skin actively **metabolized** labeled I. Male skin synthesized 2.5 times as much **testosterone** and twice as much androsterone as female skin. Androst-4-ene-3,17-dione was synthesized at a similar rate by male and female skin. Thus, not only the endocrine glands, but also the skin can synthesize steroids of high biol. activity from biol. less active ones. The skin converted I to I sulfate, thus it had a marked I

sulfokinase activity. Pubic skin from an agonadal man also synthesized (from I) androsterone of high radioactivity and **testosterone** of low radioactivity. Eleven radioactive **metabolites** were identified in the incubate. Androst-4-ene-3,17-dione was **metabolized** to androsterone and **testosterone** in roughly equal amts. by abdominal skin from normal females and in a ratio of 2:1 by skin from **hirsute** females. The sum of the 2 compds. was higher in **hirsute** than normal females. Human axillary sweat contained considerable amts. of keto steroid sulfate ester, mostly I and androsterone sulfate. Alterations at **enzymes** of the skin are assumed to be involved in some cases of idiopathic **hirsutism**.

L28 ANSWER 20 OF 20 HCAPLUS COPYRIGHT 1998 ACS
AN 1968:58086 HCAPLUS
DN 68:58086
TI Adrenal hirsutism (3.beta.-hydroxy steroid dehydrogenase deficiency). Chromatographic separation of the 17-keto steroid fraction in urine. II. Dehydroepiandrosterone-forming adrenal hyperplasia and constitutional hirutism
AU Goebel, Peter
CS Med. Univ.-Poliklin., Tuebingen, Ger.
SO Endokrinologie (1967), 52(3-4), 168-201
CODEN: ENDKAC
DT Journal
LA German
AB In adrenal cortical hyperplasia, caused by dehydroepiandrosterone (I), a disproportionately marked excretion of I occurred, although this was not as large as in adrenal cortical tumors. After an i.v. infusion of 40 units ACTH the I excretion increased moderately while less increase occurred for the 11-hydroxyandrostenedione (II) and cortisol (III) **metabolites**, 11-hydroxyandrosterone (IV) and 11-hydroxyetiocholanolone (V), resp. These **metabolites** showed an increased excretion in the steady state of the disease. Patients with constitutional **hirsutism** showed in the steady state a moderately increased I excretion (11 times normal values) which increased more markedly after administration of ACTH than in normal subjects. When ACTH was administered to normal subjects, it produced primarily III, while in the I hyperplasia patients and those with **hirsutism** a disproportionately increased amt. of I was excreted, whereas the increased excretion of II, IV, and V was less than in normal subjects. Because pregnanediol and pregnanetriol, decompn. products of the III precursor progesterone, and 17.alpha.-hydroxyprogesterone (precursor of III) could not be demonstrated in the urine, an incomplete **enzymic** blockage within this reaction chain is improbable. Probably there exists a primary defect in 3.beta.-hydroxysteroid dehydrogenase (VI) in the adrenal cortex. While patients with a constitutional **hirsutism** have a normal hypophyseal ACTH activity and only a small **enzyme** defect, patients with I hyperplasia have an increased ACTH activity, probably due to a marked **enzyme** defect with a latent III insufficiency. Furthermore, changes in steroid excretion may be due to constitutional differences. Patients with I hyperplasia as well as those with a constitutional **hirsutism** have a relatively greater I deficiency in the adrenal cortex than corresponding patients with adipositas. Thus, after the sepn. of the 17-keto steroid fraction in the urine the existence of adrenal

hirsutism (lack of VI) is easily established, while the single detn. of **testosterone** is not sufficient, because in adrenal **hirsutism testosterone** is normal or only slightly elevated. 118 references.

=> d 1-13 bib abs

L37 ANSWER 1 OF 13 MEDLINE
AN 97380971 MEDLINE
DN 97380971
TI Androgen metabolism as it affects hair growth in androgenetic alopecia.
AU Kaufman K D
CS Merck Research Laboratories, Rahway, New Jersey, USA.
SO DERMATOLOGIC CLINICS, (1996 Oct) 14 (4) 697-711. Ref: 67
Journal code: DER. ISSN: 0733-8635.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199710
EW 19971003
AB Androgens, in combination with a genetic susceptibility, have been demonstrated to be required for the development of androgenetic alopecia. Disturbances in androgen metabolism or target organ sensitivity are thought to underlie the pathophysiology of the condition. Observations of patients with disorders of androgen metabolism or function have determined the basic physiology involved in regulation of hair growth by androgens at selective body sites. More recently, in vitro studies of scalp skin and hair follicles have begun to define specific alterations in androgen metabolism at the local level that may play a key role in pathogenesis. The prominent role of 5-reductase in these studies suggests that inhibitors of this **enzyme** may provide new therapeutic opportunities for patients with androgenetic alopecia.

L37 ANSWER 2 OF 13 MEDLINE
AN 94271582 MEDLINE
DN 94271582
TI Biochemical mechanisms regulating human hair growth.
AU Sawaya M E
CS SUNY Brooklyn Health Science Center.
SO SKIN PHARMACOLOGY, (1994) 7 (1-2) 5-7. Ref: 7
Journal code: AOA. ISSN: 1011-0283.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199409
AB The human hair follicle cycles in active growth and resting phases controlled by a complex network of biochemical processes, yet to be fully understood. It is well known that hair follicles on scalp respond to androgens by a shortening of the anagen growth phase causing hairs to regress to a finer, thinner texture. The target tissue androgens, testosterone, and dihydrotestosterone can circulate systemically to skin or can be formed locally in hair follicles and sebaceous glands by specific **enzymes** in the steroid cascade. Kinetic constants have been evaluated for several

enzymes which mediate dihydrotestosterone formation, including 5a-reductase, and the cytochrome P-450 aromatase **enzyme** in isolated human hair follicles and sebaceous glands from scalp of men and women with androgenetic alopecia. The levels of these **enzymes** differed between men and women, and from frontal versus occipital sites within the same patient, indicating that similar steroid mechanisms may be taking place in men and women, but the amount or level of **enzymes** vary, perhaps explaining why men have more severe patterns of hair loss than women. Knowing the differences between men and women with androgenetic alopecia could shape more effective treatment options in the future.

L37 ANSWER 3 OF 13 MEDLINE
AN 94049475 MEDLINE
DN 94049475
TI [Virilization in women. Clinical and therapeutic aspects]. L'androgenizzazione nella donna. Aspetti clinici e terapeutici.
AU Molinatti G M; Messina M; Monaco A; Passera P
CS Cattedra di Medicina Interna, Universit`a degli Studi di Torino..
SO MINERVA ENDOCRINOLOGICA, (1993 Mar) 18 (1) 1-11. Ref: 36
Journal code: NAN. ISSN: 0391-1977.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA Italian
EM 199402
AB Androgenization in women can be divided, from a clinical standpoint, in two groups: a major form (with hirsutism, seborrhea, acne, hair loss, menstrual irregularities, masculinization of muscles and voice, mammary atrophy) and a minor one, with skin changes only (in particular hirsutism) with or without menstrual problems. The different clinical presentations are reviewed here: virilizing tumours of adrenal glands and ovaries, adrenogenital congenital syndromes, Cushing's syndrome and disease, iatrogenic forms, simple or idiopathic hirsutism, late onset **enzymatic** defects of adrenal steroidogenesis, polycystic ovary syndrome). The relevant therapeutic options are discussed. Special attention is devoted to the treatment of simple cutaneous androgenization, a problem affecting about 10% of women, by antiandrogenic drugs, mostly cyproterone acetate and spironolactone. These compounds compete with dehydrotestosterone for androgen cutaneous receptors, and have obtained good results, although not permanent. The indications, use and side-effects are also discussed.

L37 ANSWER 4 OF 13 MEDLINE
AN 92231297 MEDLINE
DN 92231297
TI Steroid chemistry and hormone controls during the hair follicle cycle.
AU Sawaya M E
CS Department of Dermatology and Biochemistry, University of Miami, School of Medicine, Florida 33101.
SO ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1991 Dec 26) 642 376-83; discussion 383-4. Ref: 20
Journal code: 5NM. ISSN: 0077-8923.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals; Cancer Journals
EM 199207
AB Human hair follicles contain several steroid **enzymes** capable of transforming weak androgens, such as dehydroepiandrosterone, into more potent target tissue androgens, such as testosterone and dihydrotestosterone. Kinetic constants have been evaluated for the 3-alpha, 3-beta, and 17-beta hydroxysteroid dehydrogenase **enzymes**, 5a-reductase, and the aromatase **enzyme** in isolated human HF from scalp of men and women with androgenetic alopecia. The apparent Km values did not differ for each **enzyme** whether present in bald, receded HF or thick, anagen HF of men or women. However, levels of specific activity varied greatly in the frontal versus occipital HF analyzed. The androgen receptor content and activation factors also differ between men and women. The steroid mechanisms influencing AGA in men and women may be similar, but differences in the specific activity/amounts of **enzymes**, receptors, and activation factors differ between men and women. These findings may explain the varied clinical presentations of men and women with AGA, and may shape treatment options for the future.

L37 ANSWER 5 OF 13 MEDLINE
AN 88285831 MEDLINE
DN 88285831
TI delta 5-3 beta-hydroxysteroid dehydrogenase activity in sebaceous glands of scalp in male-pattern baldness [see comments].
CM Comment in: J Invest Dermatol 1989 Aug;93(2):292
AU Sawaya M E; Honig L S; Garland L D; Hsia S L
CS Department of Dermatology and Cutaneous Surgery, University of Miami School of Medicine, Florida 33101.
SO JOURNAL OF INVESTIGATIVE DERMATOLOGY, (1988 Aug) 91 (2) 101-5. Journal code: IHZ. ISSN: 0022-202X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198811
AB Sebaceous glands were isolated by manual dissection using a stereomicroscope from skin specimens of bald scalp of men with male-pattern baldness undergoing hair transplant or scalp reduction surgery and also from specimens taken from hairy and bald areas of scalp at autopsy of adult male victims of accidental death within 3 h post mortem. Homogenates of the isolated glands exhibited activities of delta 5-3 beta-hydroxysteroid dehydrogenase (3 beta HSD), 17 beta-hydroxysteroid dehydrogenase, and testosterone 5 alpha-reductase by the conversion of [3H]dehydroepiandrosterone (DHA) to 3H-delta 4-androstenedione (AD), [3H]testosterone, and [3H]dihydrotestosterone. Homogenates of glands from bald (B) scalp had greater 3 beta HSD activity than homogenates of glands from hairy (H) scalp. After differential centrifugation, 3 beta HSD activity was found mainly in the microsomal and 105,000 X g supernatant fractions. Specific activity of the **enzyme** based on protein mass was highest in the microsomal fraction; however, the total 3 beta HSD activity in the 105,000 X g supernatent of B glands was significantly (p less than .01) greater than that of H glands. 3 beta HSD activity in sebaceous glands

isolated from autopsy specimens did not differ from that of glands isolated from surgical specimens in apparent Km (0.13-0.14 microM), pH optima (8.0), or coenzyme requirement for NAD. Since substantial 3 beta HSD activity was present in the cytosol, and cytosol of B glands showed increased 3 beta HSD activity, the increased conversion of DHA to AD may be a critical step for androgenic action and may be responsible for excessive androgenicity in male-pattern baldness.

L37 ANSWER 6 OF 13 MEDLINE
AN 84247195 MEDLINE
DN 84247195
TI Metabolism and concentration of androgenic steroids in the abdominal skin of women with idiopathic hirsutism.
AU Faredin I; Toth I
SO ACTA MEDICA HUNGARICA, (1984) 41 (1) 19-34.
Journal code: OY4. ISSN: 0236-5286.
CY Hungary
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198410
AB The in vitro metabolisms of [4-14C]-labelled DHA, delta 5-diol, delta 4-dione and Test were studied in skin tissue excised from the hairy hypogastric region of three patients diagnosed as suffering from "idiopathic hirsutism". The concentrations of DHA, And, delta 4-dione, delta 5-diol, Test, DHT, DHA-S, And-S, delta 5-diol-S and Test-S were determined in other portions of the same skin tissue. In the knowledge of the concentrations of the androgens and the C19-steroid sulphates in the blood and in the skin tissue, and also of the metabolisms of the main androgen precursors and Test in the hairy abdominal skin, new diagnoses can be established within the group of idiopathic hirsutisms : "pure peripheral hirsutism" and "mixed peripheral hirsutism". In the former the hyperactivity of the **enzymes** of the skin tissue takes part in the emergence of the disease form, while the latter involves the joint participation of the hyperactivity of the **enzymes** of the skin tissue and the high level of delta 4-dione in the blood. The picture of the metabolism in the hairy abdominal skin of the hirsute patients was dominated by Test formed in pathologically high amount from the precursors as a consequence of the hyperactivity of 17 beta-HSD. The formation of DHT and the activity of 5 alpha-R were of only secondary importance.

L37 ANSWER 7 OF 13 MEDLINE
AN 84166363 MEDLINE
DN 84166363
TI Androgen metabolism in hirsute patients treated with cyproterone acetate.
AU Mowszowicz I; Wright F; Vincens M; Rigaud C; Nahoul K; Mavier P; Guillemant S; Kuttenn F; Mauvais-Jarvis P
SO JOURNAL OF STEROID BIOCHEMISTRY, (1984 Mar) 20 (3) 757-61.
Journal code: K70. ISSN: 0022-4731.
CY ENGLAND: United Kingdom
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198407

AB Cyproterone acetate (CPA) in association with percutaneously administered estradiol has been used for the treatment of 150 hirsute patients for periods ranging from 6 months to 3 years. A spectacular clinical improvement ensued. Plasma testosterone (T) and androstenedione (A) fell from 69.0 +/- 24 to 33.0 +/- 8 and 210 +/- 103 to 119 +/- 25 ng/dl (mean +/- SD) respectively after 3 months of treatment and remained low thereafter. In contrast, T glucuronide (TG) and 3 alpha-androstanediol (Adiol) remained high during the whole course of treatment: 37 +/- 9 and 115 +/- 43 micrograms/24 h respectively. In vitro T 5 alpha-reductase activity (5 alpha-R) in pubic skin decreased from 147 +/- 34 to 79 +/- 17 fmol/mg skin after 1 year of treatment. To elucidate the discrepancy between plasma and urinary androgens levels, T production rate (PR) and metabolic clearance rate (MCR) were measured with the constant infusion technique in 7 patients before and after 6 months of treatment. PR decreased from 988 +/- 205 to 380 +/- 140 micrograms/24 h (mean +/- SD). In contrast MCRT increased from 1275 +/- 200 to 1632 +/- 360 1/24 h; this increase in MCRT explains the striking plasma T concentration fall and the high TG and Adiol excretion relative to the decrease in PR. Antipyrine clearance rate (n = 8) increased from 36.3 +/- 5.2 to 51.5 +/- 7.4 ml/min whereas 6 beta hydroxycortisol remained unchanged. In conclusion, CPA acts through several mechanisms: (1) it lowers the androgen input to the target cells by (a) depressing T production through its antigonadotropic effect and (b) accelerating T metabolic inactivation due to a partial **enzymatic** inducer effect on the liver; (2) at the target cell level it competes with any remaining T for the receptor binding sites; (3) the decrease in the androgen-dependent skin 5 alpha-R is a consequence of both actions of androgen suppression and androgen receptor blockade; it reinforces the antiandrogenic effect of CPA.

L37 ANSWER 8 OF 13 MEDLINE
AN 83186680 MEDLINE
DN 83186680
TI Androgen binding capacity and 5 alpha-reductase activity in pubic skin fibroblasts from hirsute patients.
AU Mowszowicz I; Melanitou E; Doukani A; Wright F; Kuttenn F; Mauvais-Jarvis P
SO JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM, (1983 Jun) 56 (6) 1209-13.
Journal code: HRB. ISSN: 0021-972X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 198308
AB We have measured the total (cytosolic plus nuclear) androgen binding capacity of pubic skin fibroblasts from nine patients with hirsutism of various origin. Confluent intact cell monolayers were incubated with increasing concentrations (0.05-2 nM) of [3H]dihydrotestosterone ([3H]DHT) with or without a 200-fold excess of unlabeled DHT. The androgen binding capacities (mean +/- SD) were similar in normal men (411 +/- 171 fmol/mg DNA), women (310 +/- 103 fmol/mg DNA), and hirsute patients (313 +/- 141 fmol/mg DNA) regardless of the plasma androgen levels. In contrast, the 5 alpha-reductase level in pubic skin fibroblasts (mean +/- SD) was, as previously described, higher in hirsute women (3.3 +/- 2.6 fmol/micrograms DNA . h) than in normal women (1.1 +/- 0.6 fmol/microgram DNA . h; P less than 0.05). We conclude from these

data that: 1) increased androgen binding capacity cannot be held responsible for hypersensitivity to androgens in hirsutism; 2) the androgen receptor is not regulated by androgens in human skin, as similar levels are observed in men, women, and hirsute patients; 3) this contrasts with 5 alpha-reductase activity and emphasizes the importance of this **enzyme** as an amplifier of androgen action in areas where it is stimulated by androgens, such as pubic skin.

L37 ANSWER 9 OF 13 MEDLINE
AN 80034314 MEDLINE
DN 80034314
TI [Adrenal hyperandrogenism due to **enzyme** disturbance of late onset (author's transl)].
Hyperandrogenies surrenaliennes par trouble **enzymatique** `a revelation tardive chez la femme.
AU Bricaire H; Luton J P; Guilhaume B; Laudat M H
SO NOUVELLE PRESSE MEDICALE, (1979 Aug 25-Sep 3) 8 (33) 2663-8.
Journal code: O5Q. ISSN: 0301-1518.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
LA French
FS Priority Journals
EM 198002
AB In the context of hyperandrogenism, the group of hyperandrogenism due to disturbances in hormon-synthesis of late onset is worthy of being considered separately, not by virtue of its prevalence but by the fact that its course may be one of isolate hirsutism (3 cases out of 11 in this study), or even sterility. The diagnosis may be of varying difficulty, because of the incomplete nature of the block. Eleven cases are reported, ten due to a partial deficit in 21 hydroxydation, and one due to a deficit in 11 hydroxydation. The presence of cortisone precursors is often more significant in stimulation tests. Estimation of blood testosterone levels may give somewhat high results in certain cases, but it must be emphasized that it may be diminished dexamethasone and the estimateion of delta 4 androstenedione is of value. In difficult cases, the diagnosis of a minor or incomplete disturbance is based upon a combination of biological, statistical and dynamic arguments. However this diagnosis is important since cortisone at low inhibitory doses are effective, in particular against menstrual disorders, sometimes making it possible to rapidly correct sterility.

L37 ANSWER 10 OF 13 MEDLINE
AN 76169525 MEDLINE
DN 76169525
TI Metabolism of androgenic steroids in human skin. pp. 507-19.
AU Julesz M
SO In: Lissak K, ed. Hormones and brain function. New York, Plenum Press, 1973. WL 300 I631H 1971, .
Journal code: IDM. Call number: WL 300 I601H 1971.
CY United States
DT Book; (MONOGRAPH)
LA English
EM 197608

L37 ANSWER 11 OF 13 MEDLINE
AN 72128708 MEDLINE
DN 72128708

TI [Some clinically relevant findings in recent research on androgens]. Einige klinisch relevante Ergebnisse der neueren Androgenforschung.
AU Tamm J; Voigt K D
SO SCHWEIZERISCHE MEDIZINISCHE WOCHENSCHRIFT. JOURNAL SUISSE DE MEDECINE, (1971 Jul 31) 101 (30) 1078-83. Ref: 31
Journal code: UEI. ISSN: 0036-7672.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA German
FS Priority Journals
EM 197207

L37 ANSWER 12 OF 13 MEDLINE
AN 71141083 MEDLINE
DN 71141083
TI Dynamics of androgen metabolism in women with hirsutism.
AU Bardin C W; Mahoudeau J A
SO ANNALS OF CLINICAL RESEARCH, (1970 Dec) 2 (4) 251-62. Ref: 68
Journal code: 53A. ISSN: 0003-4762.
CY Finland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 197106

L37 ANSWER 13 OF 13 MEDLINE
AN 69230434 MEDLINE
DN 69230434
TI [Influence of sex hormones on the metabolism of androgens]. Influence des hormones sexuelles sur le metabolisme des androg`enes.
AU Mauvais-Jarvis P; Bercovici J P; Floch H H
SO REVUE FRANCAISE D ETUDES CLINIQUES ET BIOLOGIQUES, (1969 Feb) 14 (2) 159-68.
Journal code: RZL.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
LA French
FS Priority Journals
EM 196910

=> d 1-28 bib abs

L39 ANSWER 1 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 97:208433 BIOSIS
DN 99507636
TI 19-Nor-10-azasteroids: A novel class of inhibitors for human steroid 5-alpha-reductases 1 and 2.
AU Guarna A; Belle C; Machetti F; Occhiato E G; Payne A H; Cassinai C; Comerci A; Danza G; Bellis A D; Dini S; Maurrucci A; Serio M
CS Dip. Chim. Organ., Univ. Firenze, Via Gino Capponi 9, I-50121 Firenze, Italy
SO Journal of Medicinal Chemistry 40 (7). 1997. 1112-1129. ISSN: 0022-2623
LA English
AB Steroid 5-alpha-reductase is a system of two isozymes (5-alpha-R-1 and 5-alpha-R-2) which catalyzes the NADPH-dependent reduction of testosterone to dihydrotestosterone in many androgen sensitive tissues and which is related to several human endocrine diseases such as benign prostatic hyperplasia (BPH), prostatic cancer, acne, alopecia, pattern baldness in men and hirsutism in women. The discovery of new potent and selective 5-alpha-R inhibitors is thus of great interest for pharmaceutical treatment of these diseases. The synthesis of a novel class of inhibitors for human 5-alpha-R-1 and 5-alpha-R-2, having the 19-nor-10-azasteroid skeleton, is described. The inhibitory potency of the 19-nor-10-azasteroids was determined in homogenates of human hypertrophic prostates toward 5-alpha-R-2 and in DU-145 human prostatic adenocarcinoma cells toward 5-alpha-R-1, in comparison with finasteride (IC-50 = 3 nM for 5-alpha-R-2 and apprx 42 nM for 5-alpha-R-1), a drug which is currently used for BPH treatment. The inhibition potency was dependent on the type of substituent at position 17 and on the presence and position of the unsaturation in the A and C rings. DELTA-9(11)-19-Nor-10-azaandrost-4-ene-3,17-dione (or 10-azaestra-4,9(11)-diene-3,17-dione) (4a) and 19-nor-10-azaandrost-4-ene-3,17-dione (5) were weak inhibitors of 5-alpha-R-2 (IC-50 = 4.6 and 4.4 mu-M, respectively) but more potent inhibitors of 5-alpha-LR-1 (IC-50 = 263 and 299 nM, respectively), whereas 19-nor-10-aza-5-alpha-androstane-3,17-dione (7) was inactive for both the isoenzymes. The best result was achieved with the 9:1 mixture of DELTA-9(11)- and DELTA-8(9)-17-beta-(N-tertbutylcarbamoyl)-19-nor-10-aza-4-androsten-3-one (10ab) which was a good inhibitor of 5-alpha-R-1 and 5-alpha-R-2 (IC-50 = 127 and 122 nM, respectively), with a potency very close to that of finasteride. The results of ab initio calculations suggest that the inhibition potency of 19-nor-10-azasteroids could be directly related to the nucleophilicity of the carbonyl group in the 3-position.

L39 ANSWER 2 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 97:339718 BIOSIS
DN 99638921
TI Mechanism of androgen action and role of 5-alpha-reductase.
AU Blanchard Y; Robaire B
CS Dep. Pharmacol. et Therapeutique, Univ. McGill, 3655 rue Drummond, Montreal, PQ H3G 1Y6, Canada
SO M-S (Medecine Sciences) 13 (4). 1997. 467-473. ISSN: 0767-0974
LA French
AB In the male, **androgens**, defined as C19 steroids, are synthesized by the testis and adrenal. The high lipid solubility of

androgens allows them to readily penetrate cells and bind to the intracellular **androgen** receptor. The two **androgens** that bind with high affinity to the **androgen** receptor are **testosterone** (T) and its 5-alpha-reduced **metabolite** dihydrotestosterone (DHT); other **androgens** have very weak biological activity. Binding of **androgens** to the **androgen** receptor increases the half life of the receptor several fold. Though **testosterone** is the primary **androgen** found in the circulation, DHT is the steroid that binds with highest affinity to the **androgen** receptor. The conversion of T to DHT is mediated by 5-alpha-reductase. High levels of this **enzyme** activity are found in some tissues where **androgen** action occurs, such as in the prostate and the epididymis, while it is essentially absent from others, such as the testis and muscle. Though the **enzyme** has not yet been purified to homogeneity, cDNAs from two different genes, encoded on different chromosomes, have been extensively used to understand the regulation of the mRNAs of 5-alpha-reductase. The tissue distribution of these mRNAs differs markedly in both man and rodents; type 2 5-alpha-reductase has been associated with the 5-alpha-reductase deficiency syndrome. An extensive series of studies, using the rat epididymis as a model, have revealed that the two 5-alpha-reductase mRNASs are regulated in different manners with respect to development, hormonal environment and longitudinal distribution in this tissue. It has been proposed that inhibition of this **enzyme** activity could be effective as a male contraceptive, for the treatment of **alopecia** and of benign prostatic hyperplasia (BPH) and prostatic cancer. Indeed, the first commercially available 5-alpha-reductase inhibitor, finasteride, has been marketed for the treatment of BPH. With the advent of new drugs that affect both the **androgen** receptor and 5-alpha-reductase, it should become possible to finely regulate **androgen** action.

L39 ANSWER 3 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 97:180452 BIOSIS
DN 99472165
TI Association of the steroid synthesis gene CYP11a with polycystic ovary syndrome and hyperandrogenism.
AU Gharani N; Waterworth D M; Batty S; White D; Gilling-Smith C; Conway G S; McCarthy M; Franks S; Williamson R
CS Dep. Mol. Genet., Imperial Coll. Sch. Med. St. Mary's, London W2 1PG, UK
SO Human Molecular Genetics 6 (3). 1997. 397-402. ISSN: 0964-6906
LA English
AB Biochemical data implicate an underlying disorder of **androgen** biosynthesis and/or **metabolism** in the aetiology of polycystic ovary syndrome (PCOS). We have examined the segregation of the genes coding for two key **enzymes** in the synthesis and **metabolism** of **androgens**, cholesterol side chain cleavage (CYP11a) and aromatase (CYP19, with PCOS in 20 multiply-affected families. All analyses excluded CYP19 cosegregation with PCOS, demonstrating that this locus is not a major determinant of risk for the syndrome. However, our results provide evidence for linkage to the CYP11a locus (NPL score = 3.03, p = 0.003). Parametric analysis using a dominant model suggests genetic heterogeneity, generating a maximum HLOD score of 2.7 (a = 0.63). An association study of 97 consecutively identified Europids with PCOS and matched controls demonstrates significant allelic association of a CYP11a 5'

UTR pentanucleotide repeat polymorphism with **hirsute** PCOS subjects (p = 0.03). A strong association was also found between alleles of this polymorphism and total serum **testosterone** levels in both affected and unaffected individuals (p = 0.002). Our data demonstrate that variation in CYP11a may play an important role in the aetiology of hyperandrogenaemia which is a common characteristic of polycystic ovary syndrome.

L39 ANSWER 4 OF 28 BIOBUSINESS COPYRIGHT 1998 BIOSIS
AN 97:35974 BIOBUSINESS
DN 0893509
TI 19-Nor-10-azasteroids: A novel class of inhibitors for human steroid 5-alpha-reductases 1 and 2.
AU Guarna A; Belle C; Machetti F; Occhiato E G; Payne A H; Cassinai C; Comerci A; Danza G; Bellis A D; Dini S; Maurrucci A; Serio M
CS Dip. Chim. Organ., Univ. Firenze, Via Gino Capponi 9, I-50121 Firenze, Italy.
SO Journal of Medicinal Chemistry, (1997) Vol.40, No.7, p.1112-1129. ISSN: 0022-2623.
DT ARTICLE
FS NONUNIQUE
LA English
AB Steroid 5-alpha-reductase is a system of two isozymes (5-alpha-R-1 and 5-alpha-R-2) which catalyzes the NADPH-dependent reduction of testosterone to dihydrotestosterone in many androgen sensitive tissues and which is related to several human endocrine diseases such as benign prostatic hyperplasia (BPH), prostatic cancer, acne, alopecia, pattern baldness in men and hirsutism in women. The discovery of new potent and selective 5-alpha-R inhibitors is thus of great interest for pharmaceutical treatment of these diseases. The synthesis of a novel class of inhibitors for human 5-alpha-R-1 and 5-alpha-R-2, having the 19-nor-10-azasteroid skeleton, is described. The inhibitory potency of the 19-nor-10-azasteroids was determined in homogenates of human hypertrophic prostates toward 5-alpha-R-2 and in DU-145 human prostatic adenocarcinoma cells toward 5-alpha-R-1, in comparison with finasteride (IC-50 = 3 nM for 5-alpha-R-2 and apprx 42 nM for 5-alpha-R-1), a drug which is currently used for BPH treatment. The inhibition potency was dependent on the type of substituent at position 17 and on the presence and position of the unsaturation in the A and C rings. DELTA-9(11)-19-Nor-10-azaandrost-4-ene-3,17-dione (or 10-azaestra-4,9(11)-diene-3,17-dione) (4a) and 19-nor-10-azaandrost-4-ene-3,17-dione (5) were weak inhibitors of 5-alpha-R-2 (IC-50 = 4.6 and 4.4 mu-M, respectively) but more potent inhibitors of 5-alpha-LR-1 (IC-50 = 263 and 299 nM, respectively), whereas 19-nor-10-aza-5-alpha-androstane-3,17-dione (7) was inactive for both the isoenzymes. The best result was achieved with the 9:1 mixture of DELTA-9(11)- and DELTA-8(9)-17-beta-(N-tertbutylcarbamoyl)-19-nor-10-aza-4-androsten- 3-one (10ab) which was a good inhibitor of 5-alpha-R-1 and 5-alpha-R-2 (IC-50 = 127 and 122 nM, respectively), with a potency very close to that of finasteride. The results of ab initio calculations suggest that the inhibition potency of 19-nor-10-azasteroids could be directly related to the nucleophilicity of the carbonyl group in the 3-position.

L39 ANSWER 5 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 96:316393 BIOSIS
DN 99038749

TI Predominant expression of 5-alpha-reductase type 1 in pubic skin from normal subjects and hirsute patients.
AU Mestayer C; Berthaut I; Portois M-C; Wright F; Kuttenn F; Mowszowicz I; Mauvais-Jarvis P
CS Lab. Biochim. B, Hop. Necker, 149 rue de Sevres, 75749 Paris Cedex 15, France
SO Journal of Clinical Endocrinology & Metabolism 81 (5). 1996. 1989-1993. ISSN: 0021-972X
LA English
AB Dihydrotestosterone (DHT), the 5-alpha-reduced **metabolite** of **testosterone**, is the active molecule triggering **androgen** action, and 5-alpha-reductase (5-alpha-R), the **enzyme** converting **testosterone** to DHT, is a key step in this mechanism. Skin, like prostate, is a DHTdependent tissue. Our laboratory demonstrated, many years ago, that 5-alpha-R in external genitalia was not regulated by **androgens**, whereas it was **androgen** dependent in pubic skin. As two genes, 5-alpha-R types 1 and 2, encoding for 5-alpha-R **enzymes** have been recently cloned, we undertook the present study to determine whether the two **enzymes** we had postulated on the basis of regulation studies were coincident with the cloned isoforms. The expression of the two isoforms was studied in genital and pubic skin fibroblasts from normal men, normal women, and **hirsute** patients. Messenger ribonucleic acid analysis, using Northern blot and RT-PCR techniques, indicated that both 5-alpha-R1 and -2 messenger ribonucleic acids are expressed in genital skin as well as in pubic skin fibroblasts. In contrast, studies using specific inhibitors of 5-alpha-R1 (LY 306089) and 5-alpha-R2 (finasteride) showed that 5-alpha-R2 **enzymatic** activity is predominant in genital skin, whereas 5-alpha-R1 is predominant in pubic skin of normal men, normal women, and **hirsute** patients. These data raise the question of the possible use of specific 5-alpha-R1 inhibitors in the treatment of idiopathic **hirsutism**.

L39 ANSWER 6 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 97:20577 BIOSIS
DN 99319780
TI The 5-alpha-reductase system and its inhibitors.
AU Chen W; Zouboulis C C; Orfanos C E
CS Dep. Dermatol., University Medical Cent. Benjamin Franklin, Free University Berlin, Hindenburgdamm 30, D-12200 Berlin, Germany
SO Dermatology (Basel) 193 (3). 1996. 177-184. ISSN: 1018-8665
LA English
AB 5-alpha-Reductase, the **enzyme** system that **metabolizes testosterone** into dihydro-**testosterone**, occurs in two isoforms. The type I isozyme is composed of 259 amino acids, has an optimal pH of 6-9 and represents the 'cutaneous type'; it is located mainly in sebocytes but also in epidermal and follicular keratinocytes, dermal papilla cells and sweat glands as well as in fibroblasts from genital and non-genital skin. The type 2 isozyme is composed of 254 amino acids, has an optimal pH of about 5.5 and is located mainly in the epididymis, seminal vesicles, prostate and fetal genital skin as well as in the inner root sheath of the hair follicle and in fibroblasts from normal adult genital skin. The genes encoding type 1 and type 2 isozymes are found in chromosomes 5p and 2p, respectively, and each consists of 5 exons and 4 introns. During the last decade, several steroid analogues and non-steroid agents have been developed to interfere

with 5-alpha-reductase activity. Finasteride, which has a higher affinity for the type 2 isozyme, is the first 5-alpha-reductase antagonist clinically introduced for treatment of benign prostate hyperplasia. The clinical evaluation of finasteride or other 5-alpha-reductase inhibitors in the field of dermatology has been very limited; in particular, those that selectively bind to type 1 isozyme (e.g. MK-386, LY191704) may be regarded as candidates for treatment of **androgen**-dependent skin disorders such as seborrhoea. acne, **hirsutism** and/or **androgenetic alopecia**.

L39 ANSWER 7 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 96:333472 BIOSIS
DN 99055828
TI Messenger RNA expression of steroidogenesis **enzyme** subtypes in the human pilosebaceous unit.
AU Courchay G; Boyera N; Bernard B A; Mahe Y
CS Hair Biol. Res. Group, L'Oreal, Cent. Rech. C. Zviak, F-92583 Clichy Cedex, France
SO Skin Pharmacology 9 (3). 1996. 169-176. ISSN: 1011-0283
LA English
AB In order to define the respective involvement of steroidogenesis **enzymes** subtypes in the control of hair follicle homeostasis, we evaluated, by semiquantitative RT/PCR, the expression levels of mRNAs coding for 17-beta-hydroxysteroid dehydrogenase type 1 and type 2, 3-beta-hydroxysteroid dehydrogenase, Cyt.P450-aromatase, steroid 5-alpha-reductase type 1 and type 2 and 11-beta-hydroxysteroid dehydrogenase. These assays were performed for several components of the pilosebaceous unit (PSU); fresh plucked anagen hairs, sebaceous glands and primary culture of dermal papilla, as well as other tissues involved in an active steroid **metabolism** (human testis, liver, placenta, prostate, ovary, uterus and adrenals) as controls. We found that plucked hair (i.e. mainly keratinocytes from the inner and outer root sheaths) expressed: (1) very high levels of 17-beta-hydroxysteroid dehydrogenase type 2 corresponding to levels found in liver and placenta; (2) high levels of steroid 5-alpha-reductase type 1 corresponding to levels found in testis, liver and ovary, and moderate levels of 17-beta-hydroxysteroid dehydrogenase type 1, which corresponded to the expression in testis, prostate and uterus. In contrast, Cyt.P450-aromatase, 3-beta-hydroxysteroid dehydrogenase and steroid 5-alpha-reductase type 2 were poorly expressed in the pilosebaceous unit as compared with other tissues. Interestingly, expression patterns of these **enzymes** in primary cultures of dermal papilla were distinctive since 5-alpha-reductase type 1 and 11-beta-hydroxysteroid dehydrogenase were the only mRNA detected. Taken together, these results suggest that not only sebaceous gland but also outer root sheath keratinocytes may contribute, through the activity of the steroid 5-alpha-reductase type 1, to the pathogenesis of **androgen**-dependent **alopecia**.

L39 ANSWER 8 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 96:322774 BIOSIS
DN 99045130
TI 5-alpha-Reductases and their inhibitors.
AU Spera G; Lubrano C
CS Dep. Med. Physiopathol., Univ. Rome "La Sapienza", Viale del Policlinico, 00161 Rome, Italy
SO International Journal of Immunopathology and Pharmacology 9 (1).

1996. 33-38. ISSN: 0394-6320
LA English
AB 5-alpha reductase is a key **enzyme** in **androgen** **metabolism**. Altered **enzyme** function and/or regulation is responsible for numerous human pathologies such as benign prostatic hyperplasia, acne, **hirsutism** and male pattern baldness. In order to block **androgen** action through inhibition of this **enzyme**, numerous compounds have been synthesized during the past two decades. Among them, 4-azasteroids and in particular finasteride have been extensively studied and used in the treatment of human diseases.

L39 ANSWER 9 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 1
AN 95:390879 BIOSIS
DN 98405179
TI The **enzyme** and inhibitors of 4-ene-3-oxosteroid 5-alpha-oxidoreductase.
AU Li X; Chen C; Singh S M; Labire F
CS Med. Chem. Div., Lab. Molecular Endocrinol., C.H.U.L. Res. Cent., Laval Univ., 2705 Laurier Blvd., Quebec G1V 4G2, Canada
SO Steroids 60 (6). 1995. 430-441. ISSN: 0039-128X
LA English
AB Since evidence of 5-alpha-reductase activity in rabbit liver homogenate was discovered in 1954, the presence of this **enzyme** has been demonstrated in many other organs and tissues of mammalian species. 5-alpha-Reductase selectively transforms a 4-ene-3-oxosteroid (e.g., **testosterone**) irreversibly to the corresponding 5-alpha-3-oxosteroid (e.g., 5-alpha-dihydrotestosterone) in the presence of NADPH as an essential coenzyme at an optimal pH. However, excessive production of 5-alpha-dihydrotestosterone is the major cause of many **androgen**-related disorders, such as prostate cancer, benign prostatic hyperplasia, acne, female **hirsutism**, and male pattern baldness; therefore, inhibition of **androgenic** action by 5-alpha-reductase inhibitors is a logical treatment. During the past two decades, research has focused on understanding the biological functions and effects of 5-alpha-reductase and its 5-alpha-reduced **metabolites**: purification of the **enzyme**, substrates, and **metabolites**; characterization of their physical, chemical, and biochemical properties; analysis of the amino acid sequence of the **enzyme** ; synthesis of various classes of molecules as potential inhibitors; and examination of the biological activity of the inhibitors in vitro an-omega-r in vivo. This review summarizes the biochemical studies on this **enzyme**, suggests the mechanisms of action of the **enzyme** or inhibitors, and discusses the chemistry necessary for the preparation, structure-activity relationships, and in vitro and/or in vivo data obtained from the evaluation of nonsteroidal and steroidal compounds that have been tested as inhibitors of 5-alpha-reductase. In particular, IC-50 and K-i values for relevant compounds will be compared according to molecular class. This review could function as a comprehensive working reference of what research has been accomplished so far and what problems remain to be solved in the future for those engaged in this interesting field.

L39 ANSWER 10 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 95:532068 BIOSIS
DN 98546368
TI Early polycystic ovary-like syndrome in girls with central precocious

puberty and exaggerated adrenal response.
AU Lazar L; Kauli R; Bruchis C; Nordenberg J; Galatzer A; Pertzelan A
CS Inst. Pediatr. Adolescent Endocrinol., Child. Med. Cent. Israel, Beilinson Med. Campus, Kaplan St., Petah Tiqva 49202, Israel
SO European Journal of Endocrinology 133 (4). 1995. 403-406. ISSN: 0804-4643
LA English
AB Exaggerated adrenal response (ExAR), i.e. hypersecretion of both 17-hydroxypregnenolone (17OHPreg) and 17-hydroxyprogesterone(17OHP) in response to adrenocorticotropic hormone (ACTH) stimulation, is frequently found in women with polycystic ovary (PCO) syndrome who had precocious adrenarche. In an earlier study we found an abnormal adrenal response in girls with idiopathic true central precocious puberty (CPP) at early stages of puberty. On follow-up it was noted girls with a history of CPP. Included were 49 girls with a history of CPP, 34 of whom were treated with gonadotropin-releasing hormone (GnRH) analog. All 49 were evaluated at full maturity, at ages 3/4 clinical signs of PCO (irregular menses, hirsutism, acne and obesity) and were defined as PCO-like+, whereas 29 did not fulfil the criteria and were considered PCO-like -. Girls with a definite **enzyme** deficiency were excluded from the study. All participants underwent a combined iv ACTH-GnRH test at early follicular phase. The PCO-like + girls all revealed ExAR, i.e. an elevated stimulated 17OHPreg of 6 3.4 +- 9.6 nmol/l (normal 2 8.6 +- 9.2 nmol/l) and a normal stimulated 17OHPreg/17OHP ratio of 7.1 +- 1.8 (normal 6.2 +- 2.7). whereas all the PCO-like - had a normal adrenal response (30.0 +- 8.7 and 5.3 +- 2.0 nmol/l, respectively). Compared to the PCO-like - girls, those with PCO-like+ had significantly higher levels of testosterone (1.8 +- 0.7 vs 1.0 +- 0.5 nmol/l; p lt 0.001), androstenedione (6.6 +- 3.2 vs 4.7 +- 1.8 nmol/l; p lt 0.02) and dehydroepiandrosterone sulfate (7.8 +- 4.7 vs 4.2 +- 2.5 mu-mol/l; p lt 0.004), and a trend toward inappropriate luteinizing hormone secretion. The prevalence of ExAR (40.8%) in the mature CPP girls (confined to only PCO-like +) was similar to that previously found by us in another group of girls with CPP at early puberty (44.6%). In conclusion, our findings indicate that the pattern of adrenal response remains unchanged from early puberty to adulthood and is probably inherent. As only the girls with CPP who developed early PCO syndrome showed ExAR, it is suggested that ExAR in early puberty may serve as a predictive marker for the eventual development of PCO.

L39 ANSWER 11 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 95:123291 BIOSIS
DN 98137591
TI Clinical relevance of testosterone and dihydrotestosterone metabolism in women.
AU Rittmaster R S
CS Room 809, Gerard Hall, 5303 Morris Street, Halifax, NS B3J 1B6, Canada
SO American Journal of Medicine 98 (1 PART A). 1995. 17S-21S. ISSN: 0002-9343
LA English
AB **Androgens** are part of normal female physiology. When they are secreted in excess or when they cause unwanted symptoms such as **hirsutism** and male-pattern baldness, the term hyperandrogenism is used. In many hyperandrogenic women, there is no well-defined hormonal abnormality, but the women are simply on one end of a normal spectrum of **androgen** secretion and cutaneous **androgen** sensitivity. To be active in the skin,

testosterone must be converted to dihydrotestosterone by the **enzyme** 5-alpha-reductase. **Androgen** sensitivity is determined, in part, by 5-alpha-reductase activity in the skin. This is a localized phenomenon, and there is no generalized increase in 5-alpha-reductase activity in these women. Dihydrotestosterone can be converted to glucuronide and sulfate conjugates, including androstanediol glucuronide. These **androgen** conjugates have been proposed to be serum markers of cutaneous **androgen** **metabolism**, but recent evidence indicates that they arise from adrenal precursors and are more likely to be markers of adrenal steroid production and **metabolism**. Antiandrogens (**androgen** receptor blockers) are the best medical treatment of cutaneous hyperandrogenism. 5-alpha-Reductase inhibitors have recently been approved for the treatment of benign prostatic hyperplasia, and research is currently underway to determine their effectiveness in treating **hirsutism** and male-pattern baldness.

L39 ANSWER 12 OF 28 WPIDS COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 94-034728 [04] WPIDS
CR 97-033940 [02]
DNC C94-015984
TI Fatty acid inhibition of 5-alpha reductase **enzyme** - use in diagnosing and treating disorders associated with excessive androgenic activity.
DC B05
IN LIANG, T; LIAO, S
PA (ARCH-N) ARCH DEV CORP; (ARCH-N) ARCH DEV CO
CYC 20
PI WO 9401100 A1 940120 (9404)* EN 50 pp
RW: BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
W: JP
EP 652749 A1 950517 (9524) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
US 5422371 A 950606 (9528) 27 pp
JP 08501771 W 960227 (9643) 59 pp
TW 290457 A 961111 (9711)
EP 652749 A4 970409 (9735)
ADT WO 9401100 A1 WO 93-US4090 930430; EP 652749 A1 EP 93-910950 930430, WO 93-US4090 930430; US 5422371 A CIP of US 92-889589 920527, US 92-904443 920701; JP 08501771 W WO 93-US4090 930430, JP 94-503286 930430; TW 290457 A TW 92-105407 920708; EP 652749 A4 EP 93-910950
FDT EP 652749 A1 Based on WO 9401100; JP 08501771 W Based on WO 9401100
PRAI US 92-904443 920701; US 92-889589 920527
AN 94-034728 [04] WPIDS
CR 97-033940 [02]
AB WO 9401100 A UPAB: 971030
Fatty acids of formulae (IA)-(IF). Also claimed is method of regulating 5-alpha-reductase activity, comprising treating a target organ or tissue with a fatty acid cpd. (C) method for diagnosing disorders associated with excessive **androgenic** activity, (AA), or of analysing factors involved in regulation of AA, comprising (a) measuring the amt. of a prodn. (q) formed due to excessive **androgenic** activity (b) administering any cpd. mentioned in (A), including exclusions, and the additional cpds. below; and (c) measuring the amt. of (Q) again; (d) method of treating cancer comprising treating the tissue or organ with a fatty acid.
USE/ADVANTAGE - The claimed and excluded fatty acids repress

androgenic activity. They are used in treatment of prostatic hyerplasia and cancer, acne, **hirsutism**, male pattern baldness, and seborrhoea. It is also expected that some cpds. may regulate steroid **metabolism**, in turn affecting the function of normal and mutated steroid hormone receptors, including **androgen** or other hormone sensitive or insensitive disorders or tumours, or in action mechanism studies. The cpd. is opt. used in the form of a cosmetic compsn. for topical application. The cpds. are stabilised against **metabolism** degradation and incorporation into lipid or other structures by fluorination, alkylation and cyclisation. They can produce fewer side effects than hormonal therapies which indiscriminately inhibit all **androgen** actions.

Dwg.1,5/19

ABEQ US 5422371 A UPAB: 950721

Selectively inhibiting 5-alpha-reductase in intact cells comprises admin. of a 14-22C unsatd. aliphatic fatty acid or alcohol to prevent redn. of androgen. Fatty acid pref. has 1-6 double bonds e.g. docosahexaenoic acid. Fatty alcohol is e.g. palmitoleyl alcohol.

Also claimed is a method for inhibiting 5-alpha-reductase activity by determining a lower rate of conversion of testosterone to 5-alpha-DHT.

USE - Inhibiting 5-alpha-reductase in the treatment of excessive growth of an androgen-responsive argon or tissue e.g. excessive pigmentation. Also for treating prostatic hyperplasia, prostatic cancer, hirsutism, acne, male pattern baldness and seborrhoea.

Dwg.0/15

L39 ANSWER 13 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS

AN 94:551162 BIOSIS

DN 98010710

TI Clinical and hormonal effects of the 5-alpha-reductase inhibitor finasteride in idiopathic hirsutism.

AU Moghetti P; Castello R; Magnani C M; Tosi F; Negri C; Armanini D; Bellotti G; Muggeo M

CS Cattedra Malattie del Metabolismo, Ospedale Policlinico, I-37134 Verona, Italy

SO Journal of Clinical Endocrinology & Metabolism 79 (4). 1994. 1115-1121. ISSN: 0021-972X

LA English

AB Hyperactivity of 5-alpha-reductase in the skin is considered a major mechanism of excessive **hair growth** in **hirsute** women with normal levels of serum **androgens** (idiopathic **hirsutism**). Preventing the conversion of **testosterone** to dihydrotestosterone by inhibiting 5-alpha-reductase activity could thus be the most rational and effective treatment in this condition. The present study evaluated the effects of the oral administration of finasteride (5 mg once daily) for 6 months in 17 young women with idiopathic **hirsutism**, 5 of whom were also given an oral contraceptive. The degree of **hirsutism** (graded by a modified Ferriman-Gallwey score), serum sex hormone levels, and serum and urinary 5-alpha-**metabolism** steroid profiles were determined basally and periodically during the treatment period. The modified Ferriman-Gallwey score showed a remarkable reduction after 6 months of finasteride treatment (5.9 +- 0.6 us. 11.7 +- 1.3; P lt 0.01). Serum 5-alpha-dihydrotestosterone and 3a-androstanediol glucuronide

levels were decreased, and urinary C-19 and C-21 5-beta/5-alpha **metabolite** ratios were increased compared with pretreatment values. No significant adverse effect was reported. In women treated with finasteride and oral contraceptive, clinical efficacy was slightly more pronounced. In conclusion, the 5-alpha-reductase inhibitor finasteride is well tolerated and seems to be a useful toot in the treatment of idiopathic **hirsutism**.

L39 ANSWER 14 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 93:163352 BIOSIS
DN BA95:84402
TI ANDROSTERONE SULFATE PHYSIOLOGY AND CLINICAL SIGNIFICANCE IN HIRSUTE WOMEN.
AU ZWICKER H; RITTMASTER R S
CS ROOM 809, GERARD HALL, 5303 MORRIS STREET, HALIFAX, NOVA SCOTIA, B3J 1B6 CANADA.
SO J CLIN ENDOCRINOL METAB 76 (1). 1993. 112-116. CODEN: JCEMAZ ISSN: 0021-972X
LA English
AB Androsterone sulfate (Andros-S) is the most abundant 5.alpha.-reduced **androgen metabolite** in serum. To determine whether this steroid could serve as a marker of 5.alpha.-reductase activity, we developed a specific RIA, using tritiated Andros-S to assess procedural losses. Baseline serum Andros-S levels (.mu.mol/L; mean .+-. SEM) in 14 **hirsute** women (3.0 .+-. 0.4) were not reduced by ovarian suppression with leuprolide (3.0 .+-. 0.3), but were decreased by 79% with combined ovarian and adrenal suppression with leuprolide and dexamethasone. The mean Andros-S level in polycystic ovarian syndrome (3.2 .+-. 0.4) and in idiopathic **hirsutism** (3.5 .+-. 0.5) was not significantly different from levels in normal women (3.0 .+-. 0.5), but were significantly greater than levels in obese women (1.7 .+-. 0.3; $P < 0.05$). The serum concentrations of Andros-S were about 10-fold greater than those of androsterone glucuronide and 100-fold greater than those of androstanediol glucuronide. Serum Andros-S concentrations correlated strongly with dehydroepiandrosterone sulfate ($R = 0.59$; $P < 0.001$) and to a lesser degree with androstanediol glucuronide and androsterone glucuronide ($R = 0.28$ and 0.49, respectively). There was a weak correlation with androstenedione levels and the androstenedione response to ACTH ($R = 0.38$ and 0.34, respectively), and no significant correlation with serum **testosterone** ($R = 0.19$). The ratio of an;y of the 5.alpha.-reduced products (Andros-S, androstanediol glucuronide, and androsterone glucuronide) to precursors (androstenedione and **testosterone**) was not increased in **hirsute** women, suggesting that these women did not have a generalized increase in 5.alpha.-reductase activity. In conclusion, these results confirm that Andros-S is the most abundant 5.alpha.-reduced **androgen metabolite** in serum. It is primarily, if not exclusively, of adrenal origin in **hirsute** women. The fact that its levels were not elevated in **hirsutism**, although those of other adrenal **androgens** and **androgen metabolites** (androstanediol glucuronide and androsterone glucuronide) were, suggests that variations in **sulfotransferase** activity or **metabolic** clearance of Andros-S may be important determinants of serum Andros-S levels. Although Andros-S may be a marker of systemic 5.alpha.-reductase activity, there was no evidence of a generalized increase in 5.alpha.-reductase activity in **hirsute** women. Andros-S is therefore not recommended as a

marker of either adrenal **androgen** production or of **hirsutism**.

L39 ANSWER 15 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 92:146684 BIOSIS
DN BA93:80909
TI PROSTATES PATES AND PIMPLES THE POTENTIAL MEDICAL USES OF STEROID 5-ALPHA REDUCTASE INHIBITORS.
AU TENOVER J S
CS DIV. GERONTOLOGY GERIATRIC MED., DEP. MED., EMORY UNIVERSITY SCH. MED., WESLEY WOODS HOSP., 1821 CLIFTON ROAD NE, ATLANTA, GA. 30329-5102.
SO ENDOCRINOL METAB CLIN NORTH AM 20 (4). 1991. 893-910. CODEN: ECNAER ISSN: 0889-8529
LA English
AB The steroid 5.alpha.-reductase **enzyme** is responsible for the formation of DHT from testosterone. DHT has been the major androgen implicated in the pathogenesis of benign prostatic hyperplasia, male pattern baldness, acne, and idiopathic female hirsutism. Although specific inhibitors of 5.alpha.-reductase are not yet generally available for human use, it is expected that they will become available within the next several years. Based on biochemical, histologic, and anatomic information from animals given 5.alpha.-reductase inhibitors, preliminary data on their use in humans, and knowledge gained from men with the inherited 5.alpha.-reductase deficiency, it is expected that these 5.alpha.-reductase inhibitors may have a major role in the medical management of benign prostatic hyperplasia. In addition, it is possible that these compounds will hold promise for the prevention of male pattern baldness and for the treatment of resistent acne and idiopathic hirsutism.

L39 ANSWER 16 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 91:351799 BIOSIS
DN BR41:36314
TI THE UBIQUITOUS POLYCYSTIC OVARY.
AU FRANKS S
CS REPRODUC. ENDOCRINOL. GROUP, DEP. OBSTETRICS AND GYNECOL., ST. MARY'S HOSP. MED. SCH., LONDON W2 1PG.
SO J ENDOCRINOL 129 (3). 1991. 317-320. CODEN: JOENAK ISSN: 0022-0795
LA English

L39 ANSWER 17 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 90:224329 BIOSIS
DN BA89:121619
TI INCREASE IN PLASMA 5-ALPHA ANDROSTANE-3-ALPHA 17-BETA-DIOL GLUCURONIDE AS A MARKER OF PERIPHERAL ANDROGEN ACTION IN HIRSUTISM A SIDE EFFECT INDUCED BY CYCLOSPORIN A.
AU VEXIAU P; FIET J; BOUDOU P; VILLETTE J-M; FEUTREN G; HARDY N; JULIEN R; DREUX C; BACH J-F; CATHELINEAU G
CS HOPITAL SAINT LOUIS, 1 RUE CLAUDE VELLEFAUX, 75475 PARIS CEDEX 10, FR.
SO J STEROID BIOCHEM 35 (1). 1990. 133-138. CODEN: JSTBBK ISSN: 0022-4731
LA English
AB Dose-dependent hypertrichosis is a common dermatological side-effect affecting the majority of patients treated with cyclosporine A (CSA). Previous studies have not demonstrated the influence of CSA on specific sex hormone levels. The aim of this study is to investigate

whether CSA increases the activity of 5.alpha.-reductase, an **enzyme** which transforms **androgens** into dihydrotestosterone in peripheral tissues. The **metabolite** which best reflects this activity is 5.alpha.-androstane-3.alpha.,17.beta.-diol glucuronide (Adiol G). The study was carried out on 49 insulin-dependent diabetes patients participating in the double-blind "Cyclosporine-Diabete-France" clinical trial, of which 28 were treated with CSA (16 males and 12 females), and 21 received only placebo (10 males and 11 females). All patients underwent extensive clinical and laboratory evaluations prior to and during the present study. In addition to Adiol G, **testosterone** (T), dehydroepiandrosterone sulfate (DHEA S) and sex hormone-binding globulin (SHBG) were assayed. Levels of Adiol G increased significantly in CSA-treated groups: males, 11.86 .+-. 2.58 vs 7.83 .+-. 2.30 nmol/l; females, 4.48 .+-. 2.70 vs. 2.10 .+-. 1.22 nmol/l; $P < 0.02$ (comparison of means). There were no significant differences in this parameter before and during treatment in either the male or female placebo groups (paired t-test). During the treatment period, T, DHEA S, SHBG and the T/SHBG ratio did not significantly change with respect to their baseline values in any of the groups studied (comparison of means). Comparison (using paired t-test) showed a significant increase of DHEA S in CSA-treated groups: males, .delta. = 3.08 nmol/l, $P < 0.01$; females, .delta. = 0.98 .+-. 1.13 nmol/l, $P < 0.05$. In conclusion, it is positive that CSA induces hypertrichosis or **hirsutism** by increasing 5.alpha.-reductase activity in peripheral tissues. Nevertheless the role of increased DHEA S as a possible Adiol G precursor cannot be excluded.

L39 ANSWER 18 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 90:52490 BIOSIS
DN BA89:29854
TI TESTOSTERONE ESTRADIOL BINDING GLOBULIN TEBG IN HIRSUTE PATIENTS TREATED WITH CYPROTERONE ACETATE CPA AND PERCUTANEOUS ESTRADIOL.
AU VINCENS M; MERCIER-BODARD C; MOWSZOWICZ I; KUTTENN F; MAUVAIS-JARVIS P
CS HOP. NECKER, 149 RUE SEVRES, 75743 PARIS CEDEX, FRANCE.
SO J STEROID BIOCHEM 33 (4 PART A). 1989. 531-534. CODEN: JSTBBK ISSN: 0022-4731
LA English
AB **Testosterone**-estradiol binding globulin (TeBG) was studied in 50 **hirsute** women, before and after 6-month treatment with cyproterone acetate (CPA). 50 mg CPA was administered orally from the 5th to the 25th day of the menstrual cycle and combined with 3 mg 17.beta.-estradiol (E2) administered percutaneously from days 16-25 of the cycle. TeBG was evaluated by a filter assay measuring [3H]-DHT binding capacity. Before treatment, the mean plasma TeBG level was 40 .+-. 12 nM in **hirsute** patients, which is significantly lower than TeBG value in normal women (60 .+-. 9 nM, n = 20, $P < 0.010$) and intermediate between normal women and normal men (30 .+-. 8 nM, N = 20). After a 6-month treatment, TeBG strikingly decreased to 22 .+-. 8 nM, which is significantly lower than pretreatment values ($P < 0.01$) and even less than TeBG level in normal men. Parallel TeBG assay by immunoelectrodiffusion in 8 of these **hirsute** patients provided similar results. With this treatment, plasma **testosterone** and .delta.4-androstenedione, measured between the 20th and 25th days of the cycle, decreased from 68 .+-. 21 to 25 .+-. 8 ng/dl, and 210 .+-. 95 to 98 .+-. 31 ng/dl respectively. Plasma estradiol decreased from 150 .+-. 62 pg/ml to 75 .+-. 25 pg/ml. In contrast, urinary

3.alpha.-androstanediol glucuronide remained high: 112 .+-. 51 and 123 .+-. 55 .mu.g/24 h respectively before and with CPA treatment. Three mechanisms have been proposed to explain TeBG decrease under CPA + E2 perc. treatment (1) relative competition of CPA with labelled DHT in the TeBG-binding capacity assay, (2) relative hypoestrogenism with this treatment, (3) a progestagen or even a partial agonistic **androgen** effect of of CPA on TeBG synthesis in the liver. The third mechanism appears to be predominant. In any case, TeBG decrease combined with the partial **enzymatic** induction effect of CPA on the liver contributes to the increase in the **metabolic** clearance rate of T and the high urinary Adiol levels previously reported with CPA treatment.

L39 ANSWER 19 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 87:380749 BIOSIS
DN BA84:67246
TI IS INCREASED 5-ALPHA REDUCTASE ACTIVITY A PRIMARY PHENOMENON IN ANDROGEN-DEPENDENT SKIN DISORDER.
AU DIJKSTRA A C; GOOS M A A; CUNLIFFE W J; SULTAN C; VERMORKEN A J M
CS INSERM U 58, BIOCHIM. STEROIDES, 60 RUE NAVACELLES, 34100 MONTPELLIER, FRANCE.
SO J INVEST DERMATOL 89 (1). 1987. 87-92. CODEN: JIDEAE ISSN: 0022-202X
LA English
AB **Testosterone metabolism** was investigated in fractions of human skin, enriched in epidermis, dermis, sebaceous glands, and sweat glands, by histologic sectioning of skin punch biopsies, and the results were compared with two culturable skin cells, i.e., keratinocytes and fibroblasts. Since sebocytes could not be brought in culture, **metabolism** was also investigated in the hamster flank model. In the epidermal tissue of the skin biopsies the predominant **metabolite** was androstenedione, formed by the **enzyme** 17.beta.-hydroxysteroid dehydrogenase. The same was true for cultured hair follicle keratinocytes. In the deeper skin layers the formation of androstenedione was markedly reduced, whereas the formation of 5.alpha.-reduced **metabolites** was highly increased, with a maximum in the skin fractions containing large sebaceous glands. Cultured shoulder skin fibroblasts showed a markedly different **testosterone metabolism** compared with the sectioned skin biopsies, suggesting that dermal fibroblasts play a less important role in the overall skin **testosterone metabolism**. The present approach, allowing the comparison of **testosterone metabolism** in different substructures of the same skin biopsy provides new evidence that the high 5.alpha.-reductase activity in the specific skin fractions must be mainly ascribed to the sebaceous glands. These results render a previous hypothesis, stating that the elevated level of 5.alpha.-reductase and subsequent formation of dihydrotestosterone in **androgenetic alopecia** and acne (usually accompanied by seborrhea) could therefore simply be the consequence of sebaceous gland enlargement, much stronger. This hypothesis is further evaluated by quantitative correlation of sebaceous gland size with **enzyme** activity in the hamster flank model.

L39 ANSWER 20 OF 28 WPIDS COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 86-293020 [45] WPIDS
CR 85-154304 [26]; 85-231782 [38]; 88-163221 [24]; 89-131755 [18]; 91-059684 [09]; 91-059685 [09]
DNC C86-126931
TI New 3-methyl-4-hydroxy-5-propyl-7 -halo-benzofuran-2-carboxylate

cpds. - useful as lipoxygenase inhibitors, leukotriene biosynthesis inhibitors, antiinflammatories, analgesics and cyto-protectives.

DC B02

IN ATKINSON, J G; GUINDON, Y; LAU, C K; RASMUSSON, G H; REYNOLDS, G F

PA (MERI) MERCK FROSST CANADA INC; (MERI) MERCK & CO INC

CYC 10

PI EP 200443 A 861105 (8645)* EN 22 pp
R: CH DE FR GB IT LI NL
JP 62053980 A 870309 (8715)
US 4663347 A 870505 (8720)
US 4745127 A 880517 (8822)
EP 200443 B 890301 (8909) EN
R: CH DE FR GB IT LI NL
DE 3662194 G 890406 (8915)
US 4822803 A 890418 (8918)
US 4933351 A 900612 (9031)

ADT EP 200443 A EP 86-302952 860418; JP 62053980 A JP 86-88423 860418; US 4663347 A US 85-725265 850419; US 4745127 A US 87-1262 870107; US 4822803 A US 88-152215 880204; US 4933351 A US 89-303784 890130

PRAI US 83-547508 831031; US 84-584061 840227; US 84-661645 841017; US 85-725265 850419; US 85-800624 851121; US 87-1262 870107; US 88-152215 880204

AN 86-293020 [45] WPIDS

CR 85-154304 [26]; 85-231782 [38]; 88-163221 [24]; 89-131755 [18]; 91-059684 [09]; 91-059685 [09]

AB EP 200443 A UPAB: 941021
3-Methyl-4-hydroxy-5-propyl- 7-R''-benzofuran-2-carboxylate derivs. of formula (I) and their pharmaceutically acceptable salts are new, where R' is phenyl or methyl; and R'' is F or Cl. Also claimed are compsns. contg. (a) (I) and (b) a non-steroidal antiinflammatory agent (pref. indomethacin), a peripheral analgesic, a cyclooxygenase inhibitor, a leukotriene antagonist, an antistiminic, a prostaglandin inhibitor, or a thromboxane antagonist.

USE - (I) are lipoxy genase inhibitors with superior activity to the cpds. specifically disclosed in EP-146243. (I) can be used to treat erosive gastritis; erosive oesophagitis; inflammatory bowel disease, ethanol induced haemmorrhagic erosion; hepatic ischaemia; noxious agent induced damage or necrosis of hepatic, pancreatic, renal or myocardial tissue, liver parenchymal damage caused by hepatoxic agents such as CCl4 and D-galactosanine; ischaemic renal failure; disease induced hepatic damage; bile salt induced pancreatic or gastric damage; trauma or stress induced cell damage; and glycerol induced renal failure. (I) are potent inhibitors of the 5-lipoxygenase pathway of arachidonic acid metabolism and have little or no inhibiting effect or the cyclooxygenase pathway.
Dwg.0/0
Dwg.0/0

ABEQ EP 200443 B UPAB: 930922
A compound having the general formula (I) where R' is phenyl or methyl and R'' is fluorine or chlorine or a pharmaceutically acceptable salt of such a compound.

ABEQ US 4663347 A UPAB: 930922
Benzofuran-2-carboxylic acid esters of formula (I) and salts are new. In (I), R-R4 are specifically chosen in each cpd. from R is H or 7-F or 7-Cl; R1 is Me, Pr, Ph; R2 is OH, OMe, OEt, OPh, OiPr, or gp. (i); R3 is 4-, 5- or 6-OH, 4- or 5-Ac, 5-NHAc, gp. (ii); R4 is H, 5-Pr, 5-CH2OH, 5-CH2OEt, 4- and 5-CH2CH=CH2, 5-NPr or gp. (iii). Esp. cpds. include R is H, R1 is Me, R2 is O-iPr, R3 is 4-OH, R4 is H. (I) may be prepd. e.g. by reacting alkoxide (II) with

ethyl-2-bromo acetate to (III), which may be cyclised to benzofuran carboxylate (IV), hydrolysed to (V), and derivatised.

USE - (I) inhibit mammalian leukotriene biosynthesis by inhibiting 5-lipooxygenase and preventing **metabolism** of arachidonic acid to the leukotrienes. Used to treat pulmonary conditions, inflammation, skin diseases, asthma, allergies, and some cardiovascular disorders. Dosage e.g. 0.002-100 (0.02-30) mg/kg/day.

ABEQ US 4745127 A UPAB: 930922

Benzyl esters of benzofuran-2-carboxylic acids of formula (Id) and (I) and salts are new. In (Id), R1 is H, 1-6C alkyl, Ar1(1-3C)alkyl, Ar1 or CH2OH; R3, R4, and T are each H, 1-4C alkyl 2-4C alkenyl, -(CH2)mM, with m is 0 or 1 and M is OR5, halo, CF3, SR5, Ar1, COOR6, C(O)R12 with R12 is H, 1-6C alkyl or Ar1; NHC(O)R7, OC(O)R7, SC(O)R7, OC(S)R7, NR8R9, NHSO2R10 where R10 is 1-6C alkyl, Ph, p-tolyl or CF3; SOR5, CONR8R9, SO2NR8R9, SO2R5, NO2 or CN or any two of R3, R4 and T may be joined to form 5- or 6-membered satd. ring contg. 0, 1 or 2, 0 atoms, the other being C; each R5 is H, 1-6C alkyl, Bz, Ar1, perfluoro(1-4C)alkyl, CH2R11 where R11 is 1-5C alkyldimethylamino, OH(2-5C)alkyl, CH2COOR6, or CH2COOR7; each R6 is H or 1-6C alkyl; each R7 is 1-6C alkyl, Bz, Ar1, NR8R9, NHAr1 or O(1-4C)alkyl; each R8 and each R9 is H, 1-6C alkyl or R8 and R9 together with attached N may be 5-8 ring heterocycloalkyl; each Ar1 is 1- or 2-naphthyl, Ph opt. mono- or di-substd.

USE - (I) inhibit 5-lipoxygenase and leukotriene synthesis by preventing arachidonic acid **metabolism** and are used in treatment of asthma, allergies, inflammation, skin diseases, and cardiovascular disorders, etc. opt. with non-steroidal anti-inflammatoies (indomethacin).

ABEQ US 4822803 A UPAB: 930922

(+17.10.84, 27.2.84, 21.11.85, 19.4.85, 7.1.87-US-661645, 584061, 800624, 725265, 001262) Benzofuran 2-carboxylic acid hydrazide have formula (I) and opt. comprises its pharmaceutical salt. Pref. R1 is e.g. H, (1-6C) alkyl, aryl, (1-3C) alkyl or CH2OH, etc. R3 and R4 are each e.g. H, (1-4C) alkyl, 2-4C) alkenyl or (CH2)nM; n is 0 or 1; M is e.g. halogen, CF3, aryl, etc.; and R2 is e.g. p-NO2 substd. PhNHNH, p-MeO-subtsd. PhNHNH, PhNHNH, etc.

USE - To inhibit mammalian 5-lipoxygenase **enzyme** and prevent **metabolism** of arachidonic acid to leukotrienes in treatment of asthma, allergic disorders, inflammation, skin diseases and cardiovascular disorders.

ABEQ US 4933351 A UPAB: 930922

Benzofuran-3-carboxamides of formula (I) and salts are new. In (I) R is Me, Ph, Pr, R2 is pyridyl, NHPh, NHPh-p-No2, NHPh-p-OMe, heterocyclists etc. R3 is 4-OH, 4-OAC, 5- and 6-OH and -OAc, 4- and 6--O-C(O)OMe, R4 is H, 5-Pr, 5-CH2CH=CH2.

USE - Inhibition of leucotyriene biosynthesis by inhibiting 5-lipoxygenase and arachidonic acid **metabolism**. Used to treat pulmonaryy conditions, inflammation, cardiovascular and skin conditions.

ABEQ US 5151429 A UPAB: 930922

17beta-Acyl-4-aza-5alpha -androst-1-en-3-ones of formula (I) are new. In (I) R is H, Me, or Et; R2 is benzyl, PhEt, 2- or 4-pyridyl, 2-pyrrolyl, 2-furyl or PhS; and R' R'' and R''' are each H or Me.

Typical cpds. are 17beta-(2-pyrrolylcarbonyl) -4-aza-5alpha-androst-1-en-3-one and its 4-methyl deriv. Prepn. is e.g. from steroid ester (A).

USE - The cpds. with R' is H or Me; R'' is H or beta-Me; and R''' is H, alpha- or beta-Me are **testosterone** 5-alpha reductase inhibitors. (I) with R', R'' and R''' each H are used to

treat the hyperandrogenic conditions of acne, seborrhea, female **hirsutism**, and benign prostatic hypertrophy. Dosage is e.g. 50-2000 mg.
0/0

L39 ANSWER 21 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 85:342728 BIOSIS
DN BA80:12720
TI COMBINED 21 HYDROXYLASE AND 11-BETA HYDROXYLASE DEFICIENCY IN FAMILIAL CONGENITAL ADRENAL HYPERPLASIA.
AU HURWITZ A; BRAUTBAR C; MILWIDSKY A; VECSEI P; MILEWICZ A; NOVAT D; ROSLER A
CS SECT. ENDOCRINOLOGY METABOLISM, CHILDREN'S HOSPITAL 678 WILLIAM AVE., WINNIPEG, MANIT. R3E 0W1, CAN.
SO J CLIN ENDOCRINOL METAB 60 (4). 1985. 631-638. CODEN: JCEMAZ ISSN: 0021-972X
LA English
AB Studies in 3 families (A, B, and C) revealed 5 patients with congenital adrenal hyperplasia (CAH) due to partial and combined 21- and 11.beta.-hydroxylase deficiency. One patient (A-11 1), a 23-yr-old severely virilized chromosomal female, was reared as a male, and 2 females (B-11 2 and C-1) complained only of **hirsutism**, acne, and menstrual abnormalities. Patients A-11 2 and B-11 8 (17.5 and 10 yr old) were asymptomatic and detected by finding an HLA genotype identical to that of their respectively affected brother and sister. Three patients (A-11 1, A-11 2, and C-1) had moderate hypertension. In spite of the wide range of clinical manifestations, all individuals had elevated **androgen** levels, while cortisol secretion was severely impaired only in A-11 2021-Hydroxylase deficiency was diagnosed on the basis of markedly increased plasma and urinary levels of 17-hydroxyprogesterone (17-OHP) and 21-deoxycortisol and their respective urinary **metabolites** pregnanetriol and pregnanetriolone. Plasma renin activity was elevated in 3 patients, while urinary aldosterone was normal or increased. 11.beta.-Hydroxylase deficiency was diagnosed on the basis of increased 11-deoxycortisol and deoxycorticosterone in plasma and tetrahydro-11-deoxycortisol and deoxycorticosterone in urine, particularly after ACTH administration. In contrast to classical 11.beta.-hydroxylase deficiency CAH, urinary 18-hydroxycorticosterone and 18-hydroxy-11-deoxycorticosterone were normal or elevated. The nature and mechanism of a combined **enzymatic** defect are unknown. The coincidental presence in a single individual of the mutant genes for both 21- and 11.beta.-hydroxylase deficiency CAH is very unlikely to occur. Two alternative hypotheses may explain our findings. One is the existence of a genetically inherited abnormal (or aberrant) 11.beta.-hydroxylase, whose affinity for its normal substrate is changed for an abnormal one (17-OHP). As a result, 11.beta.-hydroxylation of 11-deoxycortisol is deficient while 17-OHP 11.beta.-hydroxylation is markedly enhanced. Thus, both 11-deoxycortisol and 21-deoxycortisol as well as their urinary **metabolites** accumulate. The ability for 18-hydroxylase is not deficient, yet 21-deoxycortisol cannot be further hydroxylated to cortisol, since this steroid is not a suitable substrate for the **enzyme**. Such a disorder may represent a new allelic variant of 11.beta.-hydroxylase deficiency CAH, which, similar to 21-hydroxylase deficiency, is completely linked to the HLA complex. A 2nd explanation is partial deficiency of both **enzymes**, 1 of which is congenital (21-hydroxylase) and the other one acquired

(11.beta.-hydroxylase), as a result of the inhibitory effect of increased **androgens** on 11.beta.-hydroxylation.

L39 ANSWER 22 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 84:309593 BIOSIS
DN BA78:46073
TI **ANDROGEN METABOLISM** IN **HIRSUTE** PATIENTS TREATED WITH CYPROTERONE ACETATE.
AU MOWSZOWICZ I; WRIGHT F; VINCENS M; RIGAUD C; NAHOUL K; MAVIER P; GUILLEMANT S; KUTTENN F; MAUVAIS-JARVIS P
CS SERVICE BIOCHIM., FAC. MED. PITIE-SALPETRIERE, 91 BD DE L'HOSP., 75634 PARIS CEDEX 13, FR.
SO J STEROID BIOCHEM 20 (3). 1984. 757-762. CODEN: JSTBBK ISSN: 0022-4731
LA English
AB Cyproterone acetate (CPA) in association with percutaneously administered estradiol was used for the treatment of 150 **hirsute** patients for periods ranging from 6 mo. to 3 yr. A spectacular clinical improvement ensued. Plasma **testosterone** (T) and androstenedione (A) fell from 69.0 .+-. 24 to 33.0 .+-. 8 and 210 .+-. 103 to 119 .+-. 25 ng/dl (mean .+-. SD), respectively, after 3 mo. of treatment and remained low thereafter. In contrast, T glucuronide (TG) and 3.alpha.-androstanediol (Adiol) remained high during the whole course of treatment: 37 .+-. 9 and 115 .+-. 43 .mu.g/24 h, respectively. In vitro T 5.alpha.-reductase activity (5.alpha.-R) in pubic skin decreased from 147 .+-. 34 t 79 .+-. 17 fmol/mg skin after 1 yr of treatment. To elucidate the discrepancy between plasma and urinary **androgen** levels, T production rate (PR) and **metabolic** clearance rate (MCR) were measured with the constant infusion technique in 7 patients before and after 6 mo. of treatment. PR decreased from 988 .+-. 205 to 380 .+-. 140 .mu.g/24 h (mean .+-. SD). In contrast MCRT increased from 1275 .+-. 200 to 1632 .+-. 360 1/24 h; this increase in MCRT explains the striking plasma T concentration fall and the high TG and Adiol excretion relative to the decrease in PR. Antipyrine clearance rate (no. = 8) increased from 36.3 .+-. 5.2 to 51.5 .+-. 7.4 ml/min while 6.beta.-hydroxycortisol remained unchanged. In conclusion, CPA acts through several mechanisms; it lowers the **androgen** input to the target cells by depressing T production through its antigonadotropic effect and accelerating T **metabolic** inactivation due to a partial **enzymatic** inducer effect on the liver; at the target cell level it competes with any remaining T for the receptor binding sites; the decrease in the **androgen** -dependent skin 5.alpha.-R is a consequence of both actions of **androgen** suppression and **androgen** receptor blockade; it reinforces the antiandrogenic effect of CPA.

L39 ANSWER 23 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 85:277519 BIOSIS
DN BA79:57515
TI **METABOLISM** AND CONCENTRATION OF **ANDROGENIC** STEROIDS IN THE ABDOMINAL SKIN OF WOMEN WITH IDIOPATHIC **HIRSUTISM.**
AU FAREDIN I; TOTH I
CS H-6701 SZEGED, P.O. BOX 469, HUNGARY.
SO ACTA MED HUNG 41 (1). 1984. 19-34. CODEN: AMEHDS
LA English
AB The in vitro **metabolisms** of [4-14C]-labeled DHA [dehydroepiandrosterone], .DELTA.5-diol [5-androstene-3.beta.,

17.beta.-diol] , .DELTA.4-dione [4-androstene-3,17-dione] and test [**testosterone**] were studied in skin tissue excised from the hairy hypogastric region of 3 patients diagnosed as suffering from idiopathic **hirsutism**. The concentrations of DHA, And [androsterone], .DELTA.4-dione, .DELTA.5-diol, Test, DHT [dihydrotestosterone], DHA-S [sulfate], And-S, .DELTA.5-diol-S and Test-S were determined in other portions of the same skin tissue. In the knowledge of the concentrations of the **androgens** and the C19-steroid sulfates in the blood and in the skin tissue, and also of the **metabolism** of the main **androgen** precursors and Test in the hairy abdominal skin, new diagnoses can be established within the group of idiopathic **hirsutisms**: pure peripheral **hirsutism** and mixed peripheral **hirsutism** . In the former the hyperactivity of the **enzymes** of the skin tissue takes part in the emergence of the disease form, while the latter involves the joint participation of the hyperactivity of the **enzymes** of the skin tissue and the high level of .DELTA.4-dione in the blood. The picture of the **metabolism** in the hairy abdominal skin of the **hirsute** patients was dominated by Test formed in a pathologically high amount from the precursors as a consequence of the hyperactivity of 17.beta.-HSD [17.beta.-hydroxysteroid dehydrogenase]. The formation of DHT and the activity of 5.alpha.-R [5.alpha.-reductase] were of only secondary importance.

L39 ANSWER 24 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 82:295096 BIOSIS
DN BA74:67576
TI 3-ALPHA 17-BETA ANDROSTANEDIOL GLUCURONIDE IN PLASMA A MARKER OF ANDROGEN ACTION IN IDIOPATHIC HIRSUTISM.
AU HORTON R; HAWKS D; LOBO R
CS SECT. ENDOCRINOL., DEP. MED. OBSTET. GYNECOL., UNIV. SOUTHERN CALIF., SCH. MED., LOS ANGELES, CALIF. 90033.
SO J CLIN INVEST 69 (5). 1982. 1203-1206. CODEN: JCINAO ISSN: 0021-9738
LA English
AB Biologically active **androgens** and peripheral **androgen metabolites** in plasma were measured in 25 women with idiopathic **hirsutism** (IH). Plasma **testosterone** was not significantly elevated. Free **testosterone**, however, was increased although the elevation was not impressive (10.9 .+-. 6.6 SD vs. 3.3 .+-. 1.5 ng/dl) and one-fourth of the cases had normal unbound **testosterone**. Dihydrotestosterone (DHT) values were elevated (23.5 .+-. 14 vs. 12.5 .+-. 3.59) but again over half of the values were within the normal range. In the series of mild to moderate cases, 3.alpha.-diol was not at all discriminatory. However, plasma 3.alpha.-diol glucuronide was markedly increased (604 .+-. 376 vs. 40 .+-. 10 ng/dl), and elevated in all but 1 mild case. Previous studies document that DHT is the important **androgen** in skin and formation of DHT and 3.alpha.-diol is markedly increased in vitro in IH. Since 3.alpha.-diol glucuronide is derived largely from extrasplanchnic events, .beta.-glucuronidase is present in skin, and **androgen** stimulates formation of the **enzyme** in extrasplachnic tissue, 3.alpha.-diol glucuronide apparently is a marker of peripheral **androgen** action and markedly elevated in IH.

L39 ANSWER 25 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 83:190929 BIOSIS
DN BA75:40929

TI MULTIPLE ANDROGENIC ABNORMALITIES INCLUDING ELEVATED FREE TESTOSTERONE IN HYPER PROLACTINEMIC WOMEN.
AU GLICKMAN S P; ROSENFIELD R L; BERGENSTAL R M; HELKE J
CS UNIV. CHICAGO, WYLER CHILDREN'S HOSPITAL, 5825 S. MARYLAND AVE., BOX 118 CHICAGO, ILLINOIS 60637.
SO J CLIN ENDOCRINOL METAB 55 (2). 1982. 251-257. CODEN: JCEMAZ ISSN: 0021-972X
LA English
AB To investigate the basis of the **hirsutism** and elevated plasma dehydroepiandrosterone (DHA) and/or DHA sulfate (DHAS) in hyperprolactinemic women, **androgen** binding parameters and an extensive profile of plasma **androgens** in normal (NL) and hyperprolactinemic women (HYPRL) were measured. ACTH tests and dexamethasone (dex) suppression tests were performed in subgroups. Free **testosterone** levels were higher in HYPRL (13.1 .+-. 2.3 vs. 7.18 .+-. 0.72 pg/ml; P < 0.025), although total **testosterone** was comparable. This disparity was related to plasma **testosterone**-estradiol-binding globulin (TEBG) levels being 1/3 lower in HYPRL (mean .+-. SE, 27.4 .+-. 4.0 nM) than in NL (41.2 .+-. 3.7 nM; P < 0.0125). Less striking elevations of plasma DHAS, androstenedione and 11-deoxycortisol were found in HYPRL. Plasma total dihydrotestosterone (tDHT) was nearly 30% lower in HYPRL (11.2 .+-. 2.6 ng/dl) than in NL (15.6 .+-. 1.3 ng/dl; P < 0.025), whereas free DHT was normal. Ratios of tDHT to precursors were lower in HYPRL (P < 0.005). After ACTH stimulation, hyperresponsiveness of 17-hydroxyprogesterone and androstenedione were observed. Apparent adrenal **enzyme** efficiencies, judged from post-ACTH product to precursor ratios, were normal in HYPRL with 1 exception: the ratio of tDHT to total **testosterone** at 4 h was lower (P < 0.05). Dex suppression normalized **androgens** and obliterated the abnormal tDHT to precursor ratios. These findings suggest an ACTH dependency of the abnormalities. About 40% of HYPRL have an **androgenic** abnormality, and the most characteristic abnormality is an elevated free **testosterone** level (abnormal in 43%). Depressed TEBG and high DHAS levels were found with lesser frequency (19-21%). The plasma tDHT concentration was low, both in absolute terms and relative to its precursors. Dex suppressibility of the hyperandrogenemia was also observed. PRL may exert multiple effects on steroid secretion and **metabolism**. Possibilities include the inhibition of the TEBG level.

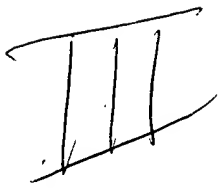
L39 ANSWER 26 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 81:238402 BIOSIS
DN BA72:23386
TI ANDROGEN METABOLISM IN HUMAN SKIN.
AU KUTTENN F; MAUVAIS-JARVIS P
CS SERVICE D'ENDOCRINOL. ET DE GYNECOL. MED., HOPITAL NECKER, 149 RUE DE SEVRES, 75730 PARIS CEDEX 15, FRANCE.
SO INT J COSMET SCI 3 (1). 1981. 9-22. CODEN: IJCMDW ISSN: 0142-5463
LA French
AB In human beings, **androgen metabolism** is important in mediating the action of male hormones upon target structures of the skin. Human skin is capable of transforming inactive steroids supplied through the blood, such as androstenedione and dehydroisoandrosterone, into the active **androgen testosterone**. Human skin is able to reduce **testosterone** to 5.alpha.-dihydrotestosterone, an essential prerequisite, during embryogenesis, for the male differentiation of target structures derived from urogenital sinus. At puberty,

hair growth in sexual areas of skin also requires the transformation of **testosterone** to dihydrotestosterone. Regulation of 5.alpha.-reductase activity varies according to the anatomical site of the **enzyme**. In fetuses, 5.alpha.-reductase activity present in tissues derived from the urogenital tract does not seem to be **androgen**-dependent, since it is acquired before the onset of **testosterone** secretion by fetal testis. The **enzyme** that mediates development of certain secondary sex characteristics, such as pilosebaceous gland activity in sexual areas, is clearly **androgen**-dependent, since it is absent before puberty and in persons with hypogonadism. The differences in the control of the 5.alpha.-reductase activity mediating the appearance of either primary or secondary sex characteristics are important and may explain the differences in 5.alpha.-reductase activity observed in adult skin of both sexes derived from different sexual areas. The knowledge of **androgen** relation to the skin is necessary to understand the action of the anti-**androgens**, particularly the compounds which may be used by topical administration.

L39 ANSWER 27 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 81:217006 BIOSIS
DN BA72:1990
TI LATE DIAGNOSIS HYPER ANDROGENISM DUE TO ADRENAL **ENZYME** DEFICIENCY.
AU HAZARD J; GUILHAUME B; REQUEDA E; PERLEMUTER L; CENAC A; BERNHEIM R
CS SERVICE D'ENDOCRINOLOGIE, HOPITAL HENRI-MONDOR, 51, AVENUE DE LATTRE-DE-TASSIGNY, 94010 CRETEIL CEDEX.
SO SEM HOP PARIS 56 (47-48). 1980 (RECD. 1981). 1975-1978. CODEN: SHPAAI ISSN: 0037-1777
LA French
AB Six women aged from 17-30 yr (mean: 21 yr) were referred on account of disorders which had begun at puberty and had been present for 3-15 yr. The reasons for consulting were **hirsutism** in 5 cases and sterility in one. The patients height (1.61-1.70 m; mean: 1.64 m) and weight (54-70 kg; mean: 59 kg) were normal. Three women menstruated regularly and 3 had anovular spaniomenorrhaea. **Hirsutism** with enlargement of the clitoris (Prader's stage I) was apparent in all 6 cases. Three patients had permanent, though moderate hypertension. The biochemical changes essential to the diagnosis were as follows: in 2 women with 21-hydroxylase deficiency there was a rise in cortisol precursors (plasma 17-OH progesterone and its urinary **metabolite**, pregnanetriol). In 4 women with 11-hydroxylase deficiency urinary 17-0H corticosteroids were increased; 2 had high desoxycortisol levels. A rise in plasma desoxycortisol/cortisol ratio under tetracosactrin stimulation is of considerable diagnostic value; plasma **androgens** (**testosterone**, .DELTA. 4 androstenedione) and their urinay **metabolites** (17-ketosteroids) were increased; all abnormalities disappeared when the adrenal function was suppressed. Under dexamethasone treatment **hirsutism** became stabilized or even regressed, blood pressure values rapidly returned to normal, menstrual disorders disappeared and ovular cycles were established. Three women became pregnant and delivered on term.

L39 ANSWER 28 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 80:54664 BIOSIS
DN BR18:54664
TI ADRENAL VIRILISM.

AU VERMEULEN A; RUBENS R
CS DEP. ENDOCRINOL. METAB. DIS., ACAD. HOSP., STATE UNIV. GHENT, GHENT, BELG.
SO JAMES, V. H. T. (ED.). COMPREHENSIVE ENDOCRINOLOGY SERIES: THE ADRENAL GLAND. X+332P. RAVEN PRESS: NEW YORK, N.Y., USA. ILLUS. 0 (0). 1979. P259-282. ISBN: 0-89004-297-7
LA English



=> d bib abs 1-8

L65 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 1998 ACS
AN 1998:97672 HCAPLUS
DN 128:213280
TI Effects of valproate, phenobarbital, and carbamazepine on sex steroid setup in women with epilepsy
AU Murialdo, G.; Galimberti, C. A.; Gianelli, M. V.; Rollero, A.; Polleri, A.; Copello, F.; Magri, F.; Ferrari, E.; Sampaolo, P.; Manni, R.; Tartara, A.
CS Department of Endocrine and Metabolic Sciences, University of Genova, I-16132, Italy
SO Clin. Neuropharmacol. (1998), 21(1), 52-58
CODEN: CLNEDB; ISSN: 0362-5664
PB Lippincott-Raven Publishers
DT Journal
LA English
AB Serum levels of sex-hormones, sex-hormone binding globulin, gonadotropin, and prolactin were evaluated during the follicular and the luteal phases in 65 women with epilepsy and in 20 healthy controls. Twenty-one patients were treated with sodium valproate (VPA), 21 with phenobarbital (PB), and 23 with carbamazepine (CBZ). VPA does not **stimulate** liver microsome **enzymes**, whereas PB and CBZ do. Patients on VPA therapy showed higher body wt. and body mass index, but no significant differences in **hirsutism** score, or in ovary vol. or polycystic ovary prevalence (at ultrasound examn.). Estradiol levels were lower in all patient groups than in healthy controls in the follicular but not in the luteal phases. VPA affected luteal progesterone surge in 63.6% of cases. This effect was significantly lower in the CBZ and PB groups. Furthermore, increases in **testosterone** and .DELTA.4-androstenedione levels and in free **androgen** index, along with a higher LH-FSH ratio in the luteal phase, were obsd. in women treated with VPA. Although sex-hormone binding globulin levels were higher in CBZ and PB than in VPA-treated patients, the differences were not significant because of the wide dispersion of the carrier protein levels. Inducer antiepileptic drugs decreased dehydroepiandrosterone sulfate levels, which remained unchanged during VPA treatment. No significant differences occurred in basal gonadotropin and prolactin levels.

L65 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 1998 ACS
AN 1997:23664 HCAPLUS
DN 126:84412
TI Effect of finasteride on human testicular steroidogenesis
AU Castro-Magana, Mariano; Angulo, Moris; Fuentes, Billy; Canas, Atilio; Sarrantonio, Mary; Arguello, Raul; Vitollo, Pam
CS Department Pediatrics, Winthrop-University Hospital, Mineola, NY, 11501, USA
SO J. Androl. (1996), 17(5), 516-521
CODEN: JOAND3; ISSN: 0196-3635
PB American Society of Andrology
DT Journal
LA English
AB We studied the testicular function and some **androgen** -mediated events in 22 males (16-30 yr of age) with male pattern baldness that was treated with finasteride (10 mg once daily) for 2 yr. Patients were evaluated every 3 mo. Prostatic vol. was detd.

in six subjects by endorectal ultrasound scans. Serum gonadotropin, prostate-specific antigen (PSA), and sex hormone levels were detd. basally and periodically during the treatment period. Fourteen subjects underwent gonadal stimulation with human chorionic gonadotropin (hCG), and the gonadotropin response to gonadotropin releasing hormone (GnRH) was detd. in eight subjects, prior to and after 2 yr of therapy. Finasteride treatment resulted in an improvement in the male pattern baldness and prostatic shrinkage that was assocd. with an increase in serum **testosterone** levels (17.2 vs. 26.3 nmol/L) and a decrease in dihydrotestosterone (DHT) levels (1.45 vs. 0.38 nmol/L), causing a marked increase in that **testosterone** /DHT ratio. A significant increase in the serum levels of androstenedione (3.67 vs. 7.05 nmol/L) and estradiol (132 vs. 187 pmol/L) was also noted, whereas androstanediol glucuronide (33.3 vs. 10.7 pmol) and PSA (1.6 vs. 0.4 ng/mL) were significantly decreased. No changes in basal or stimulated levels of gonadotropin were obsd. There was a significant increase in the **testosterone** response to hCG during finasteride therapy (.DELTA.: 16.7 vs. 35.5 nmol/L) that could be explained, at least in part, by the redn. of **testosterone** metab. resulting from the blockage induced by finasteride. The decrease in the androstenedione to **testosterone** and estrone to estradiol ratios obsd. after hCG treatment, however, strongly suggests **increased** activity of the 17-ketosteroid reductase **enzyme** and an improvement of the testicular capacity for **testosterone** prodn.

L65 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 1998 ACS
AN 1990:210694 HCAPLUS
DN 112:210694
TI Increase in plasma 5.alpha.-androstane-3.alpha.,17.beta.-diol glucuronide as a marker of peripheral **androgen** action in **hirsutism**: a side-effect induced by cyclosporine A
AU Vexiau, Patrick; Fiet, Jean; Boudou, Philippe; Villette, Jean Marie; Feutren, Gilles; Hardy, Noah; Julien, Rene; Dreux, Claude; Bach, Jean Francois; Cathelineau, Gerard
CS Diabetol. Endocrinol. Dep., Hop. Saint-Louis, Paris, Fr.
SO J. Steroid Biochem. (1990), 35(1), 133-7
CODEN: JSTBBK; ISSN: 0022-4731
DT Journal
LA English
AB Dose-dependent hypertrichosis is a common dermatol. side-effect affecting the majority of patients treated with cyclosporine A (CSA). Previous studies have not demonstrated the influence of CSA on specific sex hormone levels. The aim of this study is to investigate whether CSA **increases** the activity of 5.alpha.-reductase, an **enzyme** which transforms **androgens** into dihydrotestosterone in peripheral tissues. The metabolite which best reflects this activity is 5.alpha.-androstane-3.alpha.,17.beta.-diol glucuronide (Adiol G). The study was carried out on insulin-dependent diabetes patients participating in the double-blind clin. trial. In addn. to Adiol G, **testosterone** (T), dehydroepiandrosterone sulfate (DHEA S), and sex hormone-binding globulin (SHBG) were assayed. Levels of Adiol G increased significantly in CSA-treated groups. There were not significant differences in this parameter before and during treatment in either the male or female placebo groups. During the treatment period, T, DHEA S, SHBG and the T/SHBG ratio did not significantly change with respect to their baseline values in any of

the groups studied (comparison of means). Comparison showed a significant increase of DHEA S in CSA-treated groups. Thus, it is possible that CSA induces hypertrichosis or **hirsutism** by increasing 5.alpha.-reductase activity in peripheral tissues. Nevertheless, the role of increased DHEA S as a possible Adiol G precursor cannot be excluded.

L65 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 1998 ACS
AN 1984:557471 HCAPLUS
DN 101:157471
TI **Hair** tonic containing Staphylococcus capitis enzymes
IN Yoshizumi, Hajime; Amachi, Teruo; Kusumi, Takaaki; Tanaka, Takaharu; Ishigooka, Hiroshi
PA Suntory, Ltd., Japan
SO Eur. Pat. Appl., 26 pp.
CODEN: EPXXDW
PI EP 115408 A2 19840808
DS R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE
AI EP 84-300348 19840120
PRAI JP 83-7463 19830121
DT Patent
LA English
AB A **hair** tonic for preventing dandruff and scalp itching and promoting **hair** growth contains the supernatant of a culture of S. capitis on an animal or vegetable fat or oil. The supernatant contains lipase [9001-62-1] and **testosterone** 5.alpha.-reductase [9036-43-5]. S. capitis Was cultured in a medium of soybean peptone 50, yeast ext. 5, glucose 1, and NaCl 5 g/L at 35.degree. with agitation; 1 L of this preculture was added to a mixt. of 5 L olive oil and 100 L of the same culture medium and incubated at 35.degree. for 20 h with aeration and stirring. The supernatant was mixed with 10 g NaCl and extd. with EtOAc, the ext. evapd., extd. with MeOH, the ext. evapd., extd. with C6H6-CHCl3 (1:1) and eluated with CHCl3. The eluate was concd. to obtain the active ingredient contg. enzymes and fatty acids. A **hair** tonic was prepd. from EtOH 80, active ingredient 0.2, and H2O to 100% by wt. The prepn. was effective in increasing the growth of fur in rabbits.

L65 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 1998 ACS
AN 1984:488316 HCAPLUS
DN 101:88316
TI Metabolism and concentration of **androgenic** steroids in the abdominal skin of women with idiopathic **hirsutism**
AU Faredin, I.; Toth, I.
CS First Dep. Med., Univ. Med. Sch., Szeged, H-6701, Hung.
SO Acta Med. Hung. (1984), 41(1), 19-34
CODEN: AMEHDS
DT Journal
LA English
AB The abdominal skin of 3 women with idiopathic **hirsutism** contained **increased** concns. of **androgens** and **increased enzymic** capacity for **androgen** formation when compared with skin from healthy women. Blood levels of **androgens** were normal in 1 **hirsute** woman, indicating that her **hirsutism** was entirely attributable to the altered skin metab. Blood levels of 4-androstene-3,17-dione were above normal in the other 2 **hirsute** women, indicating that their **hirsutism** derived from a combination of altered

skin metab. and high blood **androgen** levels.

L65 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 1998 ACS
AN 1975:494643 HCAPLUS
DN 83:94643
TI Adrenal function in **hirsutism**. I. Diurnal change and response of plasma androstenedione, **testosterone**, 17-hydroxyprogesterone, cortisol, LH, and FSH to dexamethasone and 1/2 unit of ACTH
AU Givens, James R.; Andersen, Richard N.; Ragland, James B.; Wiser, Winfred L.; Umstot, Edward S.
CS Cent. Health Sci., Univ. Tennessee, Memphis, Tenn., USA
SO J. Clin. Endocrinol. Metab. (1975), 40(6), 988-1000
CODEN: JCEMAZ
DT Journal
LA English
AB ACTH dependency of plasma androstenedione (A) and **testosterone** (T) was detd. in normal and **hirsute** women by measuring the magnitude of change of A and T between the time of the cortisol (F) peak and F nadir in a diurnal study. There was a diurnal rhythm of A synchronous with F in both normal and **hirsute** women. Five of 12 **hirsute** women had a greater than normal diurnal swine of A, but only 2 of the 12 had a greater than normal diurnal swing of T. Responsiveness of A and T to 1/2 unit of i.v. ACTH was detd. after dexamethasone 1 mg was given the night before. Plasma A and T were elevated in most of the **hirsute** women during acute ACTH suppression by dexamethasone, indicating ACTH-independent hypersecretion of **androgens**. Nine of 17 **hirsute** women had a greater than normal A response to ACTH. Those who had an exaggerated diurnal swing of A also had hyperresponsiveness of A secretion to ACTH. Only 2 **hirsute** women had an exaggerated T response to ACTH. Some T levels were decreased by ACTH. Seven of the 9 **hirsute** women who had an exaggerated A response to ACTH had a normal max. F response, but a greater than normal 17-hydroxyprogesterone (17-OHP) response to ACTH with a high 17-OHP to F ratio, suggesting they had mild but compensated redn. in 21-hydroxylase or 11.beta.-hydroxyase activity. Two women with hyperresponsiveness of A secretion had low F and 17-OHP responses to ACTH suggesting reduced C21 but intact C19 3.beta.-hydroxysteroid dehydrogenase-.DELTA.5,4 isomerase activity. These apparent reduced **enzyme** activities may not be congenital, but **induced** by an altered hormonal milieu such as an abnormal **androgen** -estrogen ratio. Thus, ACTH uniformly stimulated A secretion but not T secretion and .apprx.50% of the **hirsute** women had ACTH-depencent hypersecretion of A, but most of these also had concurrent ACTH-independent hypersecretion of **androgens**.

L65 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 1998 ACS
AN 1975:168418 HCAPLUS
DN 82:168418
TI **Testosterone** 5.alpha.-reduction in the skin of normal subjects and of patients with abnormal sex development
AU Kuttenn, Frederique; Mauvais-Jarvis, Pierre
CS Lab. Biol. Chem., Fac. Med. Pitie-Salpetriere, Paris, Fr.
SO Acta Endocrinol. (Copenhagen) (1975), 79(1), 164-76
CODEN: ACENA7
DT Journal
LA English

AB Human pubic skin was obtained from normal subjects and patients with abnormal sex differentiation. Skin samples (200 mg) supplemented with NADPH, were incubated for 1 hr with labeled **testosterone**. The conversion of **testosterone** to dihydrotestosterone, and 3.alpha.-, and 3.beta.-androstanediol was averaged 14.9% in 11 normal men and 3.6 in 8 normal women. In 4 children as in 4 young hypogonadotropic hypogonadal men, the conversion rate of **testosterone** to 5.alpha.-reduced metabolites was low (0.8 - 3.5%) and increased at puberty (13.5 - 19.2%). After administration of human chorionic gonadotropin for 3 months to 1 of the hypogonadal men, it reached 30.2%. Inversely, the formation of dihydrotestosterone and androstanediols from **testosterone** was suppressed in 2 men treated with large doses of estrogen. In 3 subjects with an incomplete form of testicular feminization syndrome, the conversion rate of **testosterone** to 5.alpha.-reduced metabolites was in the normal male range (6.4 - 18.3%), whereas it was low in 1 case of the complete form of the syndrome (1.5%). In 9 women with idiopathic **hirsutism**, the rate of 5.alpha.-reduced metabolites recovered from **testosterone** was close to that of normal men (13.5%). Evidently, in human subjects, there is a good correlation between **hair** growth in skin from a sexual area and the extent of **testosterone** 5.alpha.-redn. in this tissue. Such an **enzymic** activity might be **induced** by active **androgens**. Detn. of urinary 3.alpha.-androstanediol might prove of clin. interest in the evaluation of the **androgenic** status in human subjects.

L65 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 1998 ACS
AN 1968:58086 HCAPLUS
DN 68:58086
TI Adrenal **hirsutism** (3.beta.-hydroxy steroid dehydrogenase deficiency). Chromatographic separation of the 17-keto steroid fraction in urine. II. Dehydroepiandrosterone-forming adrenal hyperplasia and constitutional hirutism
AU Goebel, Peter
CS Med. Univ.-Poliklin., Tuebingen, Ger.
SO Endokrinologie (1967), 52(3-4), 168-201
CODEN: ENDKAC
DT Journal
LA German
AB In adrenal cortical hyperplasia, caused by dehydroepiandrosterone (I), a disproportionately marked excretion of I occurred, although this was not as large as in adrenal cortical tumors. After an i.v. infusion of 40 units ACTH the I excretion increased moderately while less increase occurred for the 11-hydroxyandrostenedione (II) and cortisol (III) metabolites, 11-hydroxyandrosterone (IV) and 11-hydroxyetiocholanolone (V), resp. These metabolites showed an increased excretion in the steady state of the disease. Patients with constitutional **hirsutism** showed in the steady state a moderately increased I excretion (11 times normal values) which increased more markedly after administration of ACTH than in normal subjects. When ACTH was administered to normal subjects, it produced primarily III, while in the I hyperplasia patients and those with **hirsutism** a disproportionately increased amt. of I was excreted, whereas the increased excretion of II, IV, and V was less than in normal subjects. Because pregnanediol and pregnanetriol, decompn. products of the III precursor progesterone, and 17.alpha.-hydroxyprogesterone (precursor of III) could not be

demonstrated in the urine, an incomplete enzymic blockage within this reaction chain is improbable. Probably there exists a primary defect in 3.beta.-hydroxysteroid dehydrogenase (VI) in the adrenal cortex. While patients with a constitutional **hirsutism** have a normal hypophyseal ACTH activity and only a small **enzyme** defect, patients with I hyperplasia have an **increased** ACTH activity, probably due to a marked **enzyme** defect with a latent III insufficiency. Furthermore, changes in steroid excretion may be due to constitutional differences. Patients with I hyperplasia as well as those with a constitutional **hirsutism** have a relatively greater I deficiency in the adrenal cortex than corresponding patients with adipositas. Thus, after the sepn. of the 17-keto steroid fraction in the urine the existence of adrenal **hirsutism** (lack of VI) is easily established, while the single detn. of **testosterone** is not sufficient, because in adrenal **hirsutism testosterone** is normal or only slightly elevated. 118 references.

=> d bib abs hitrn l64

L64 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 1998 ACS
AN 1998:97672 HCAPLUS
DN 128:213280
TI Effects of valproate, phenobarbital, and carbamazepine on sex steroid setup in women with epilepsy
AU Murialdo, G.; Galimberti, C. A.; Gianelli, M. V.; Rollero, A.; Polleri, A.; Copello, F.; Magri, F.; Ferrari, E.; Sampaolo, P.; Manni, R.; Tartara, A.
CS Department of Endocrine and Metabolic Sciences, University of Genova, I-16132, Italy
SO Clin. Neuropharmacol. (1998), 21(1), 52-58
CODEN: CLNEDB; ISSN: 0362-5664
PB Lippincott-Raven Publishers
DT Journal
LA English
AB Serum levels of sex-hormones, sex-hormone binding globulin, gonadotropin, and prolactin were evaluated during the follicular and the luteal phases in 65 women with epilepsy and in 20 healthy controls. Twenty-one patients were treated with sodium valproate (VPA), 21 with phenobarbital (PB), and 23 with carbamazepine (CBZ). VPA does not **stimulate** liver microsome **enzymes**, whereas PB and CBZ do. Patients on VPA therapy showed higher body wt. and body mass index, but no significant differences in **hirsutism** score, or in ovary vol. or polycystic ovary prevalence (at ultrasound examn.). Estradiol levels were lower in all patient groups than in healthy controls in the follicular but not in the luteal phases. VPA affected luteal progesterone surge in 63.6% of cases. This effect was significantly lower in the CBZ and PB groups. Furthermore, increases in **testosterone** and .DELTA.4-androstenedione levels and in free **androgen** index, along with a higher LH-FSH ratio in the luteal phase, were obsd. in women treated with VPA. Although sex-hormone binding globulin levels were higher in CBZ and PB than in VPA-treated patients, the differences were not significant because of the wide dispersion of the carrier protein levels. Inducer antiepileptic drugs decreased dehydroepiandrosterone sulfate levels, which remained unchanged during VPA treatment. No significant differences occurred in basal gonadotropin and prolactin levels.
IT **50-06-6**, Phenobarbital, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(valproate, phenobarbital, and carbamazepine effects on sex steroid setup in women with epilepsy)

=> d l66 bib abs

L66 ANSWER 1 OF 20 MEDLINE
AN 1998429407 MEDLINE
DN 98429407
TI High serum luteinizing hormone levels induce ovarian delta4 cytochrome P450c17alpha down-regulation in **hirsute** women: complete effect on 17-hydroxylase and partial effect on 17,20-lyase.
AU Rieu M; Mourrieras F; Riveline J P; Laplanche S; Both D; Kuhn J M
CS Department of Endocrinology, Saint-Michel Hospital, Paris, France.
SO EUROPEAN JOURNAL OF ENDOCRINOLOGY, (1998 Sep) 139 (3) 304-8.
Journal code: BXU. ISSN: 0804-4643.
CY ENGLAND: United Kingdom
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199812
EW 19981203
AB It is well known that normal and mildly elevated luteinizing hormone (LH) levels induce increased activity of ovarian 17-hydroxylase and 17,20-lyase, the cytochrome P450c17alpha (P450) **enzymes**. This leads to **increased** ovarian 17alpha-hydroxyprogesterone (17-OHP) and androstenedione production. In contrast, it has been shown in both in vitro and in vivo studies in animals and in in vitro studies in women that high LH concentrations have opposite effects on these enzymes. These LH down-regulating effects appear to be more marked on 17,20-lyase than on 17-hydroxylase. Finally, these LH effects have not been reported in vivo in women. Therefore, we investigated the relationships between serum LH levels and serum 17-OHP and androstenedione concentrations in 263 consecutive **hirsute** women (HW) with normal serum 17-OHP responses to acute adrenocorticotropin (ACTH) stimulation. The patterns of basal serum steroid concentrations differed according to the basal serum LH levels. Indeed, for relationships between LH and 17-OHP concentrations, a positive correlation ($P < 0.001$) was found between the levels of these parameters when LH levels ranged from 0.2 to 9.0 IU/l. Conversely, for LH levels greater than 9.0 to 21.0 IU/l, LH values were negatively correlated ($P<0.001$) with 17-OHP concentrations. Similar results were observed for relationships between LH and androstenedione levels but the LH peak level related to decreasing androstenedione concentrations was 12.0 IU/l. Finally, the mean 17-OHP level in patients with LH levels which induced marked P450 down-regulation (i.e. more than 12 IU/l) was similar to that in patients with LH levels within the normal range (i.e. less than 6 IU/l). In contrast, the mean androstenedione level in the former patients was markedly higher ($P<0.001$) than that in the latter patients. In conclusion, as previously reported in in vitro studies, this in vivo study indicates that LH induces stimulating and down-regulating effects on both ovarian delta(4)17-hydroxylase and delta(4)17,20-lyase activities as serum LH levels gradually increase. However, in contrast to in vitro studies, LH levels which induce P450 down-regulation appear to be less effective on delta(4)17,20-lyase than on delta(4)17-hydroxylase in HW. This strongly suggests that serum factors induce, in most HW, a marked increase in delta(4)17,20-lyase, but not in delta(4)17-hydroxylase, activity leading to both partial impairment

of LH-induced delta(4)17,20-lyase down-regulation and complete LH-induced delta(4)17-hydroxylase down-regulation in these patients.

=> d l66 bib abs 2

L66 ANSWER 2 OF 20 MEDLINE
AN 1998240449 MEDLINE
DN 98240449
TI Effects of valproate, phenobarbital, and carbamazepine on sex steroid setup in women with epilepsy.
AU Murialdo G; Galimberti C A; Gianelli M V; Rollero A; Polleri A; Copello F; Magri F; Ferrari E; Sampaolo P; Manni R; Tartara A
CS Department of Endocrine and Metabolic Sciences, University of Genova, Italy.
SO CLINICAL NEUROPHARMACOLOGY, (1998 Jan-Feb) 21 (1) 52-8.
Journal code: CNK. ISSN: 0362-5664.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199809
EW 19980901
AB Serum levels of sex-hormones, sex-hormone binding globulin, gonadotropin, and prolactin were evaluated during the follicular and the luteal phases in 65 women with epilepsy and in 20 healthy controls. Twenty-one patients were treated with sodium valproate (VPA), 21 with phenobarbital (PB), and 23 with carbamazepine (CBZ). VPA does not **stimulate** liver microsome **enzymes**, whereas PB and CBZ do. Patients on VPA therapy showed higher body weight and body mass index, but no significant differences in **hirsutism** score, or in ovary volume or polycystic ovary prevalence (at ultrasound examination). Estradiol levels were lower in all patient groups than in healthy controls in the follicular but not in the luteal phases. VPA affected luteal progesterone surge in 63.6% of cases. This effect was significantly lower in the CBZ and PB groups. Furthermore, increases in **testosterone** and delta 4-androstenedione levels and in free **androgen** index, along with a higher luteinizing hormone-follicle-stimulating hormone ratio in the luteal phase, were observed in women treated with VPA. Although sex-hormone binding globulin levels were higher in CBZ and PB than in VPA-treated patients, the differences were not significant because of the wide dispersion of the carrier protein levels. Inducer antiepileptic drugs decreased dehydroepiandrosterone sulfate levels, which remained unchanged during VPA treatment. No significant differences occurred in basal gonadotropin and prolactin levels.

=> d l66 bib abs 3-20

L66 ANSWER 3 OF 20 MEDLINE
AN 97247056 MEDLINE
DN 97247056
TI Lack of an ovarian function influence on the increased adrenal **androgen** secretion present in women with functional ovarian hyperandrogenism.
AU Escobar-Morreale H F; Serrano-Gotarredona J; Garcia-Robles R; Sancho J M; Varela C
CS Department of Endocrinology, Hospital Ramon y Cajal, Madrid, Spain.. hescobar@mvax.fmed.uam.es
SO FERTILITY AND STERILITY, (1997 Apr) 67 (4) 654-62.
Journal code: EVF. ISSN: 0015-0282.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199707
EW 19970701
AB OBJECTIVE: To evaluate whether ovarian function might have an influence on the adrenal hyperandrogenism present in patients with functional ovarian hyperandrogenism. DESIGN: Controlled clinical study. SETTING: Tertiary institutional hospital. PATIENT(S): Twenty-nine **hirsute** women with functional ovarian hyperandrogenism and 12 normal controls. INTERVENTION(S): The ACTH and GnRH tests were performed before and during triptorelin-induced ovarian suppression in patients. The normal women served as controls for the ACTH test. MAIN OUTCOME MEASURE(S): Basal and ACTH-stimulated steroid values. RESULT(S): All patients presented elevated T and free **androgen** index, which normalized after triptorelin. Patients with functional ovarian hyperandrogenism and adrenal hyperandrogenism, defined by elevated basal DHEAS (n = 10), presented enhanced delta 4-17, 20-lyase activity, which persisted during ovarian suppression. delta 4-17,20-lyase activity was normal in the functional ovarian hyperandrogenism patients without adrenal hyperandrogenism (n = 19). No correlation was observed between the any of the indexes of the adrenal **enzymatic** activities evaluated and plasma E2 or T. CONCLUSION(S): **Increased** adrenal delta 4-17,20-lyase activity is present in functional ovarian hyperandrogenism women with adrenal hyperandrogenism. No influence of the excess ovarian **androgens** or estrogens was found on any of the adrenal enzymatic pathways explored.

L66 ANSWER 4 OF 20 MEDLINE
AN 97116607 MEDLINE
DN 97116607
TI Effect of finasteride on human testicular steroidogenesis.
AU Castro-Magana M; Angulo M; Fuentes B; Canas A; Sarrantonio M; Arguello R; Vitollo P
CS Department of Pediatrics, Winthrop-University Hospital, Mineola, New York 11501, USA.
SO JOURNAL OF ANDROLOGY, (1996 Sep-Oct) 17 (5) 516-21.
Journal code: HB4. ISSN: 0196-3635.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English

FS Priority Journals
EM 199705
EW 19970502
AB We studied the testicular function and some **androgen** -mediated events in 22 males (16-30 years of age) with male pattern baldness that was treated with finasteride (10 mg once daily) for 2 years. Patients were evaluated every 3 months. Prostatic volume was determined in six subjects by endorectal ultrasound scans. Serum gonadotropin, prostate-specific antigen (PSA), and sex hormone levels were determined basally and periodically during the treatment period. Fourteen subjects underwent gonadal stimulation with human chorionic gonadotropin (hCG), and the gonadotropin response to gonadotropin releasing hormone (GnRH) was determined in eight subjects, prior to and after 2 years of therapy. Finasteride treatment resulted in an improvement in the male pattern baldness and prostatic shrinkage that was associated with an increase in serum **testosterone** levels (17.2 +/- 2.5 vs. 26.3 +/- 1.7 nmol/L) and a decrease in dihydrotestosterone (DHT) levels (1.45 +/- 0.41 vs. 0.38 +/- 0.10 nmol/L), causing a marked increase in that **testosterone**/DHT ratio. A significant increase in the serum levels of androstenedione (3.67 +/- 0.49 vs. 7.05 +/- 0.70 nmol/L) and estradiol (132 +/- 44 vs. 187 +/- 26 pmol/L) was also noted, whereas androstanediol glucoronide (33.3 +/- 6.4 vs. 10.7 +/- 4.5 pmol) and PSA (1.6 +/- 0.6 vs. 0.4 +/- 0.1 ng/ml) were significantly decreased. No changes in basal or stimulated levels of gonadotropin were observed. There was a significant increase in the **testosterone** response to hCG during finasteride therapy (delta: 16.7 vs. 35.5 nmol/L) that could be explained, at least in part, by the reduction of **testosterone** metabolism resulting from the blockage induced by finasteride. The decrease in the androstenedione to **testosterone** and estrone to estradiol ratios observed after hCG treatment, however, strongly suggests **increased** activity of the 17-ketosteroid reductase **enzyme** and an improvement of the testicular capacity for **testosterone** production.

L66 ANSWER 5 OF 20 MEDLINE
AN 96397211 MEDLINE
DN 96397211
TI [Finasteride: a new drug for the treatment of male **hirsutism** and **androgenetic alopecia**?].
La finasteride: un nuovo farmaco nel trattamento dell'irsutismo e dell'**alopecia androgenica** maschile?.
AU Spinucci G; Pasquali R
CS Dipartimento di Medicina interna e Gastroenterologia, Policlinico S. Orsola-Malpighi, Bologna.
SO CLINICA TERAPEUTICA, (1996 Jun) 147 (6) 305-15. Ref: 41
Journal code: DKN. ISSN: 0009-9074.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA Italian
EM 199701
EW 19970104
AB Finasteride is a drug which inhibits the transformation of **testosterone** into its active metabolite, dihydrotestosterone, in the target organs, i.e. the skin, the scalp, the liver and the prostate. In the pathogenic mechanism of

hirsutism and **androgenetic alopecia**, and important role is presumably played by alterations of the mechanisms which transform **testosterone** into dihydrotestosterone. In some conditions an increase in dihydrotestosterone has been demonstrated, due to **increased** activity of the **enzyme** 5 alpha-reductase. The effect of finasteride develops above all at the level of type II 5 alpha-reductase. Recent studies have evaluated the effect of finasteride in patients of both sexes with **hirsutism** and **androgenetic alopecia** . In women with various forms of hyperandrogenism, the use of the drug at the doses commonly used for the treatment of benign prostatic hyperplasia seems to have induced a significant reduction in the degree of **hirsutism**. Furthermore, both in animals and men with **alopecia**, the drug seems to have led to an increase in the number and an improvement in the shape of the follicles in the anagen phase, and a simultaneous decrease of dehydrotestosterone at the level of the scalp. This study represents a review of the main results obtained over the last two years and reports the prospects which the use of finasteride may have in this context.

L66 ANSWER 6 OF 20 MEDLINE
AN 96327334 MEDLINE
DN 96327334
TI [Clinical significance of **testosterone** and dihydrotestosterone metabolism in women]. Klinicko znacenje metabolizma testosterona i dihidrotestosterona u zena.
AU Korsic M
CS Zavod za endokrinologiju, dijabetes i bolesti metabolizma Klinike za unutarnje bolesti, KBC Rebro, Zagreb.
SO LIJECNICKI VJESNIK, (1996 Mar) 118 Suppl 1 21-3. Journal code: L6C. ISSN: 0024-3477.
CY Croatia
DT Journal; Article; (JOURNAL ARTICLE)
LA Serbo-Croatian
EM 199612
AB Hyperandrogenism in women refers to both excess **androgen** production and clinical manifestations of **androgen** excess. Clinical evaluation of women with hyperandrogenism is complex. The synthesis and release of **androgenic** steroid in women are normal part of adrenal and ovarian steroidogenesis. One of the classic questions concerning **androgenic** disorders concerns the source of circulating **androgens**. Relative roles of adrenal and ovary vary greatly, both can be involved. The use of gonadal or adrenal steroid administration can sometimes be used to distinguish the source of **androgen** excess. In many cases of hyperandrogenism no laboratory diagnosis of adrenal and ovarian **androgen** overproduction can be made. These patients may have **increased androgen** sensitivity due to **increased enzyme** 5 alpha-reductase activity in the skin. To be active in the skin, **testosterone** (T) must be converted to dihydrotestosterone (DHT) by the 5 alpha-reductase. The increase in DHT production is a localized phenomenon and there is no generalized **increase** in **enzyme** activity in women with hyperandrogenism. DHT is rapidly converted to other steroid metabolites including androsteron, androstanediol and their glucuronide and sulfate conjugates. Although once thought to be specific for skin conversion of T to DTH these **androgen**

conjugates reflect adrenal steroid production and metabolism. Antiandrogens (**androgen** receptor blockers) are the most effective therapeutic modalities of cutaneous hyperandrogenism. Clinical trials are in progress to determine efficacy of finasteride for the treatment of **hirsutism** and **androgenetic alopecia**. Finasteride is the first available medication of a new class of drugs that is an competitive inhibitor of 5 alpha-reductase and therefore should be beneficial for medical treatment of cutaneous hyperandrogenism.

L66 ANSWER 7 OF 20 MEDLINE
AN 95102281 MEDLINE
DN 95102281
TI Heterogeneity of late-onset adrenal 3 beta-ol-hydroxysteroid dehydrogenase deficiency in patients with **hirsutism** and polycystic ovaries.
AU Moran C; Tena G; Herrera J; Bermudez J A; Zarate A
CS Gynecologic Endocrinology Section, Hospital Luis Castelazo Ayala, Instituto Mexicano del Seguro Social, Mexico, D.F..
SO ARCHIVES OF MEDICAL RESEARCH, (1994 Autumn) 25 (3) 315-20. Journal code: BIC. ISSN: 0188-0128.
CY Mexico
DT Journal; Article; (JOURNAL ARTICLE)
LA English
EM 199504
AB Nine women with clinical features of polycystic ovarian syndrome (PCOS) were studied in order to establish the differential diagnosis with late-onset adrenal hyperplasia (LOAH). Their **hirsutism** was classified as moderate in five patients and severe in the remaining four cases. All patients had bilateral polycystic ovarian enlargement by ultrasound examination. As a control group five women with normal ovarian function without **hirsutism** were submitted to the same protocol of study. The patients studied as well as the women of the control group had basal serum determinations of pregnenolone (P5),17-hydroxypregnenolone (17-OHP5),dehydroepiandrosterone (DHEA), pregesterone (P), 17-hydroxyprogesterone (17-OHP), androstenedione (A), **testosterone** and cortisol by radioimmunoassay techniques. The basal serum levels of **androgens** showed no correlation with the severity of **hirsutism** or with the ultrasound findings. An adrenal stimulation with synthetic adrenocorticotropic hormone (ACTH) to all women was performed in order to assess their adrenal responsiveness. The analysis of the ratios between delta 5 and delta 4 steroids demonstrated a partial enzymatic blockade at the level of 3 beta-o1-hydroxysteroid dehydrogenase (3-HSD) in three patients. The blockade was particularly in the conversion of P5 to P and 17-OHP5 to 17-OHP. The lack of delta 4 steroid secretion in the presence of normal increase of delta 5 precursors following ACTH was noted. These findings confirm the clinical use of the ACTH **stimulation** test to reveal the presence of **enzymatic** alterations in adrenal steroidogenesis in some patients previously considered to have PCOS. Since it wa demonstrated that the conversion steps were affected in variable degrees, the presence of different isoenzymes of 3-HD is suggested.

L66 ANSWER 8 OF 20 MEDLINE
AN 93163222 MEDLINE
DN 93163222
TI Ovarian steroidogenic responses to gonadotropin-releasing hormone

agonist testing with nafarelin in **hirsute** women with adrenal responses to adrenocorticotropin suggestive of 3 beta-hydroxy-delta 5-steroid dehydrogenase deficiency.

AU Barnes R B; Ehrmann D A; Brigell D F; Rosenfield R L
CS Department of Obstetrics/Gynecology, University of Chicago, Pritzker School of Medicine, Illinois 60637.

NC HD-06308 (NICHD)
RR-00055 (NCRR)
RR-00055-28SL (NCRR)
SO JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM, (1993 Feb) 76 (2) 450-5.
Journal code: HRB. ISSN: 0021-972X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199305

AB Nonclassical 3 beta-hydroxy-delta 5-steroid dehydrogenase (3 beta-HSD) deficiency type of congenital adrenal hyperplasia has been hypothesized to occur in as many as 10-40% of **hirsute** women, based on the adrenal steroidogenic responses to ACTH. However, diagnostic criteria for this "late-onset" 3 beta-HSD deficiency are not clearly established. Among 40 successive hyperandrogenic women undergoing evaluation of adrenal steroidogenic responses to ACTH, 8 had responses suggestive of 3 beta-HSD deficiency. Since 3 beta-HSD is present in both the ovary and adrenal, we attempted to document the defect in the ovary by stimulating their ovarian function with a gonadotropin-releasing hormone agonist test using nafarelin (6-D-[2-naphthyl]alanine-gonadotropin-releasing hormone). The eight **hirsute** women had steroid responses to ACTH suggestive of 3 beta-HSD deficiency, namely, the values of the delta 5-steroids, 17-hydroxypregnenolone and dehydroepiandrosterone, 30 and 60 min after ACTH in each **hirsute** woman were greater than 2 SD above the normal mean. Seven of the eight **hirsute** women had at least one elevated delta 5/delta 4-steroid ratio; however, only three of the **hirsute** women had two abnormal ratios. Furthermore, the response of the delta 4-steroid androstenedione and the ratio of androstenedione to cortisol after ACTH were significantly increased in the **hirsute** women, findings not consistent with 3 beta-HSD deficiency. After nafarelin, five and six **hirsute** patients had elevated values of the delta 4-steroids androstenedione and 17-hydroxyprogesterone, respectively. No patient had an elevated delta 5/delta 4-steroid ratio after nafarelin. Thus, ovarian steroidogenic responses to nafarelin did not support the diagnosis of 3 beta-HSD deficiency. Rather, they are consistent in most cases with polycystic ovary syndrome due to dysregulation of 17-hydroxylase and 17,20-lyase activities. We propose that **increased** activity of the **enzyme** P450c17 alpha in the adrenal cortex is responsible for most of what is often termed late-onset 3 beta-HSD deficiency.

L66 ANSWER 9 OF 20 MEDLINE
AN 93047351 MEDLINE
DN 93047351
TI Investigation of adrenal function in women with oligomenorrhoea and **hirsutism** (clinical PCOS) from the north-east of England using an adrenal stimulation test.
AU Turner E I; Watson M J; Perry L A; White M C

CS Department of Gynaecology and Medicine, University of Newcastle upon Tyne Medical School, UK.
SO CLINICAL ENDOCRINOLOGY, (1992 Apr) 36 (4) 389-97.
Journal code: DCI. ISSN: 0300-0664.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199302
AB OBJECTIVE--To determine the prevalence of adrenal enzyme dysfunction in women presenting with oligomenorrhoea and **hirsutism**, two clinical features of polycystic ovary syndrome (PCOS). DESIGN--A prospective study of women attending outpatient clinics with these complaints. Androstenedione, dehydroepiandrosterone (DHEA), 17-hydroxyprogesterone (17-OHP), 11-deoxycortisol and cortisol were measured before and after overnight dexamethasone suppression and at 60 minutes after adrenal stimulation by ACTH injection. SUBJECTS--Fifty women with clinical features of PCOS and 37 control women with regular cycles and normal **hair** distribution from the catchment area of the Royal Victoria Infirmary which includes Newcastle upon Tyne, Co. Durham, Cleveland, Cumbria and Northumberland. MEASUREMENTS--Number of women with steroid responses to ACTH beyond the normal range, as defined by the responses of the control group and in previous studies. RESULTS--Nineteen women (38%) were found to have some abnormality. One woman (2%) was identified with 21-hydroxylase (21-OHase) deficiency and a second (2%) had an increase in 17-OHP compatible with the heterozygote state for 21-OHase deficiency. Four women (8%) had isolated elevations in the DHEA response consistent with minimal 3 beta-hydroxysteroid dehydrogenase (3 beta-HSD) deficiency. Thirteen women (26%) showed increases in both androstenedione and DHEA, or androstenedione alone, compatible with enhanced 17-20 lyase activity. CONCLUSIONS--Twelve per cent of the group showed evidence consistent with an adrenal **enzyme** deficiency; 26% had results in keeping with **increased** adrenal **androgen** production without an **enzyme** deficiency. These findings may be of relevance both in the pathogenesis of the features of PCOS and in determining appropriate treatment for individual patients.

L66 ANSWER 10 OF 20 MEDLINE
AN 92181190 MEDLINE
DN 92181190
TI Late-onset congenital adrenal hyperplasia in a group of hyperandrogenic women.
AU Hassiakos D K; Toner J P; Jones G S; Jones H W Jr
CS Jones Institute for Reproductive Medicine, Department of Obstetrics and Gynecology, Eastern Virginia Medical School, Norfolk, Virginia 23507..
SO ARCHIVES OF GYNECOLOGY AND OBSTETRICS, (1991) 249 (4) 165-71.
Journal code: 6YS. ISSN: 0932-0067.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199206
AB The aim of this study was to determine the prevalence of late-onset congenital adrenal hyperplasia (LOCAH) in a group of hyperandrogenic women presenting with menstrual disturbances and/or infertility. Thirty-five women were evaluated by basal hormonal profiles and

underwent ACTH stimulation testing. In this study, 17.1% of women showed evidence of partial 21-OH deficiency (21-OHD), and 5.7% 3 beta-HSD deficiency. Neither basal hormonal levels nor clinical characteristics distinguished women with LOCAH from other hyperandrogenic women. And although the mean basal 17-OH progesterone (17-OHP) level in women with 21-OHD (152 +/- 66 ng/dl) was significantly higher than levels in other **hirsute** women, 4 of 6 (67%) women with 21-OHD had normal 17-OHP levels. Thus, to identify all affected individuals with partial 21-OHD, our data suggest that hyperandrogenic women with basal unsuppressed 17-OHP levels greater than 100 ng/dl should undergo dynamic testing. With regard to partial 3 beta-HSD deficiency, basal DHEA-S levels greater than the 95th percentile of other **hirsute** women may be used to screen for this deficiency. In conclusion, LOCAH due to partial steroid enzyme deficiencies are a frequent occurrence in women who present with symptoms of hyperandrogenism and ACTH **stimulation** remains an important tool in making the diagnosis of **enzyme** deficiencies.

L66 ANSWER 11 OF 20 MEDLINE
AN 92064721 MEDLINE
DN 92064721
TI Abnormalities of 21-hydroxylase gene ratio and adrenal steroidogenesis in hyperandrogenic women with an exaggerated 17-hydroxyprogesterone response to acute adrenal stimulation.
AU Azziz R; Wells G; Zacur H A; Acton R T
CS Department of Obstetrics and Gynecology, University of Alabama, Birmingham 35294.
NC DK-32767 (NIDDK)
SO JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM, (1991 Dec) 73 (6) 1327-31.
Journal code: HRB. ISSN: 0021-972X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199203
AB One to 2% of hyperandrogenic women demonstrate a 17-hydroxyprogesterone (17-HP) level greater than 36.3 nmol/L (1200 ng/dL) after acute ACTH-(1-24) adrenal stimulation, consistent with 21-hydroxylase (21-OH) deficient late-onset adrenal hyperplasia (LOAH). The following study was undertaken to endocrinologically and genetically define hyperandrogenic patients with an exaggerated 17-HP response to ACTH stimulation, and which do not represent LOAH. Of 265 consecutive patients suffering from **hirsutism** and/or hyperandrogenic oligomenorrhea, 23 (8.7%) demonstrated a 17-HP level 30 min post stimulation greater than 9.6 nmol/L or 316 ng/dL (the upper 95th percentile in 41 eumenorrheic nonhirsute healthy control women). Seven patients or five separate families (1.8% of total) demonstrated poststimulation 17-HP levels consistent with LOAH. Of the remaining 16 patients, the net increment in 17-HP (delta 17-HP0-30) was within normal limits in seven (2.6%) and these women were assumed to have a normal 17-HP adrenocortical response superimposed on an elevated basal level of nonadrenal (e.g. ovarian) origin. In the remaining nine hyperandrogenic patients (3.4%) various abnormalities of adrenal response were noted in all but one patient, consistent with adrenal hyper-responsiveness. One patient demonstrated an 11-deoxycortisol poststimulation level greater than 3-fold the upper 95th percentile of normal, consistent with

11-hydroxylase LOAH and was excluded from further study. Six of these women were available for further genetic characterization, all Caucasian and unrelated. Three were heterozygotes for HLA-B14, three for B40, and one for B35 antigen, HLA-types associated with the inheritance of 21-OH deficiencies. Although, normally there are two 21-OH genes (a pseudogene and a functional gene) present in a 1:1 ratio, we have previously reported a high frequency of 21-OH gene ratio abnormalities in LOAH. All but one of our patients demonstrated an abnormal 21-OH gene ratio. In conclusion, 3.4% of our hyperandrogenic population demonstrated an exaggerated 17-HP increment after ACTH stimulation, not consistent with LOAH or increased extraadrenal 17-HP production. The increased prevalence of HLA alleles known to be linked to inherited defects of 21-OH function and the increased frequency in 21-OH gene ratio abnormalities suggest that a majority of these individuals may be carriers for these genetic disorders. However, the adrenocortical abnormalities noted were more consistent with a generalized hyperreactivity of the adrenal to ACTH **stimulation**, than a specific **enzyme** deficiency, implying that carrier status for 21-OH deficiency may be incidental to the hyperandrogenism.

L66 ANSWER 12 OF 20 MEDLINE
AN 91157625 MEDLINE
DN 91157625
TI Effects of ketoconazole in **hirsute** women.
AU Akalin S
CS Department of Medicine, Hacettepe University, School of Medicine, Ankara, Turkey..
SO ACTA ENDOCRINOLOGICA, (1991 Jan) 124 (1) 19-22.
Journal code: 0NC. ISSN: 0001-5598.
CY Denmark
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 199106
AB To determine the efficacy of ketoconazole in the treatment of **hirsutism**, clinical and hormonal effects of this agent were evaluated with a randomized, placebo-controlled, double-blind cross-over study design. Nine **hirsute** women were given ketoconazole (600 mg/day) or placebo for 6 months and then crossed over. The severity of **hirsutism** was assessed according to the scale of Ferriman & Gallwey. Baseline serum **testosterone** , dehydroepiandrosterone sulphate, progesterone, estradiol, basal and stimulated cortisol and 17-alpha hydroxyprogesterone were measured. Blood was also drawn for FSH and LH levels at 0,. 30, 60, and 90 min of a GnRH stimulation test. The same parameters were determined following administration of placebo or ketoconazole for 6 months. The pretreatment (28.3 +/- 0.9) and post-placebo (27.7 +/- 1.4) Ferriman-Gallwey scores were significantly higher than the post-ketoconazole score (16.6 +/- 1.3, p less than or equal to 0.01). Basal and stimulated cortisol levels were not blunted after ketoconazole, but basal and **stimulated** 17-hydroxyprogesterone levels were significantly higher, indicating sufficient **enzymatic** inhibition. Serum dehydroepiandrosterone sulphate and **testosterone** levels were significantly lowered following ketoconazole (p less than or equal to 0.05). Although E2 levels did not change significantly at

any time, E2:**testosterone** ratios were significantly higher after ketoconazole (p less than or equal to 0.01), and the LH:FSH area ratio was also significantly greater than 3 after ketoconazole. It is concluded that ketoconazole significantly alleviates **hirsutism** by inhibiting steroid synthesis.

L66 ANSWER 13 OF 20 MEDLINE
AN 90235417 MEDLINE
DN 90235417
TI Late onset adrenal hyperplasia in a group of Irish females who presented with **hirsutism**, irregular menses and/or cystic acne.
AU McLaughlin B; Barrett P; Finch T; Devlin J G
CS Department of Endocrinology, Beaumont Hospital, Dublin, Ireland.
SO CLINICAL ENDOCRINOLOGY, (1990 Jan) 32 (1) 57-64.
Journal code: DCI. ISSN: 0300-0664.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199008
AB The aims of this study were to determine the frequency of late-onset adrenal hyperplasia due specifically to 21-hydroxylase deficiency in a group of Irish women who presented at a Dublin Clinic with symptoms of hyperandrogenism, including **hirsutism**, menstrual irregularities and/or cystic acne, and to determine if those with 21-hydroxylase deficiency showed particular HLA associations. 119 women had blood samples taken basally and 1 h after an injection of 0.25 mg synacthen with the following hormones profiled: 17-hydroxyprogesterone, 11-deoxycortisol, androstenedione, **testosterone**, DHEAS and cortisol. Blood sampling was carried out between 0900 and 1000 h during the early follicular phase of the menstrual cycle (when applicable). Ninety-six subjects were new referrals to the Clinic for investigation of hyperandrogenism and 23 were acting as controls. In this study, 6% of patients showed evidence of partial 21-hydroxylase deficiency. In addition, 3 of the 6 with partial 21-hydroxylase deficiency had normal baseline levels of 17-hydroxyprogesterone, with the biochemical abnormality becoming manifest only on synacthen stimulation. Late-onset adrenal hyperplasia due to partial deficiency of this enzyme should always be considered as a possible diagnosis in women who present with symptoms of hyperandrogenism. Synacthen **stimulation** is an important diagnostic tool in elucidating partial **enzyme** deficiency as baseline 17-hydroxyprogesterone may be normal in such patients.

L66 ANSWER 14 OF 20 MEDLINE
AN 90173256 MEDLINE
DN 90173256
TI Increase in plasma 5 alpha-androstane-3 alpha,17 beta-diol glucuronide as a marker of peripheral **androgen** action in **hirsutism**: a side-effect induced by cyclosporine A.
AU Vexiau P; Fiet J; Boudou P; Villette J M; Feutren G; Hardy N; Julien R; Dreux C; Bach J F; Cathelineau G
CS Diabetology and Endocrinology Department, Hopital Saint-Louis, Paris, France.
SO JOURNAL OF STEROID BIOCHEMISTRY, (1990 Jan) 35 (1) 133-7.
Journal code: K70. ISSN: 0022-4731.
CY ENGLAND: United Kingdom

DT (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199006
AB Dose-dependent hypertrichosis is a common dermatological side-effect affecting the majority of patients treated with cyclosporine A (CSA). Previous studies have not demonstrated the influence of CSA on specific sex hormone levels. The aim of this study is to investigate whether CSA **increases** the activity of 5 alpha-reductase, an **enzyme** which transforms **androgens** into dihydrotestosterone in peripheral tissues. The metabolite which best reflects this activity is 5 alpha-androstane-3 alpha,17 beta-diol glucuronide (Adiol G). The study was carried out on 49 insulin-dependent diabetes patients participating in the double-blind "Cyclosporine-Diab`ete-France" clinical trial, of which 28 were treated with CSA (16 males and 12 females), and 21 received only placebo (10 males and 11 females). All patients underwent extensive clinical and laboratory evaluations prior to and during the present study. In addition to Adiol G, **testosterone** (T), dehydroepiandrosterone sulfate (DHEA S) and sex hormone-binding globulin (SHBG) were assayed. Levels of Adiol G increased significantly in CSA-treated groups: males, 11.86 +/- 2.58 vs 7.83 +/- 2.30 nmol/l; females, 4.48 +/- 2.70 vs 2.10 +/- 1.22 nmol/l; P less than 0.02 (comparison of means). There were no significant differences in this parameter before and during treatment in either the male or female placebo groups (paired t-test). During the treatment period, T, DHEA S, SHBG and the T/SHBG ratio did not significantly change with respect to their baseline values in any of the groups studied (comparison of means). Comparison (using paired t-test) showed a significant increase of DHEA S in CSA-treated groups: males, delta = 3.08 +/- 3.33 nmol/l, P less than 0.01; females, delta = 0.98 +/- 1.13 nmol/l, P less than 0.05. In conclusion, it is possible that CSA induces hypertrichosis or **hirsutism** by increasing 5 alpha-reductase activity in peripheral tissues. Nevertheless the role of increased DHEA S as a possible Adiol G precursor cannot be excluded.

L66 ANSWER 15 OF 20 MEDLINE
AN 84166363 MEDLINE
DN 84166363
TI **Androgen** metabolism in **hirsute** patients treated with cyproterone acetate.
AU Mowszowicz I; Wright F; Vincens M; Rigaud C; Nahoul K; Mavier P; Guillemant S; Kuttenn F; Mauvais-Jarvis P
SO JOURNAL OF STEROID BIOCHEMISTRY, (1984 Mar) 20 (3) 757-61. Journal code: K70. ISSN: 0022-4731.
CY ENGLAND: United Kingdom
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198407
AB Cyproterone acetate (CPA) in association with percutaneously administered estradiol has been used for the treatment of 150 **hirsute** patients for periods ranging from 6 months to 3 years. A spectacular clinical improvement ensued. Plasma **testosterone** (T) and androstenedione (A) fell from 69.0 +/-

24 to 33.0 +/- 8 and 210 +/- 103 to 119 +/- 25 ng/dl (mean +/- SD) respectively after 3 months of treatment and remained low thereafter. In contrast, T glucuronide (TG) and 3 alpha-androstanediol (Adiol) remained high during the whole course of treatment: 37 +/- 9 and 115 +/- 43 micrograms/24 h respectively. In vitro T 5 alpha-reductase activity (5 alpha-R) in pubic skin decreased from 147 +/- 34 to 79 +/- 17 fmol/mg skin after 1 year of treatment. To elucidate the discrepancy between plasma and urinary **androgens** levels, T production rate (PR) and metabolic clearance rate (MCR) were measured with the constant infusion technique in 7 patients before and after 6 months of treatment. PR decreased from 988 +/- 205 to 380 +/- 140 micrograms/24 h (mean +/- SD). In contrast MCRT increased from 1275 +/- 200 to 1632 +/- 360 1/24 h; this increase in MCRT explains the striking plasma T concentration fall and the high TG and Adiol excretion relative to the decrease in PR. Antipyrine clearance rate (n = 8) increased from 36.3 +/- 5.2 to 51.5 +/- 7.4 ml/min whereas 6 beta hydroxycortisol remained unchanged. In conclusion, CPA acts through several mechanisms: (1) it lowers the **androgen** input to the target cells by (a) depressing T production through its antigonadotropic effect and (b) accelerating T metabolic inactivation due to a partial **enzymatic inducer** effect on the liver; (2) at the target cell level it competes with any remaining T for the receptor binding sites; (3) the decrease in the **androgen** -dependent skin 5 alpha-R is a consequence of both actions of **androgen** suppression and **androgen** receptor blockade; it reinforces the antiandrogenic effect of CPA.

L66 ANSWER 16 OF 20 MEDLINE
AN 83289117 MEDLINE
DN 83289117
TI Exploration of **hirsutism**: elements for a strategy.
AU Caufriez A; Copinschi G; L'Hermite M; Franckson J R
SO HORMONE RESEARCH, (1983) 18 (1-3) 98-105.
Journal code: GBI. ISSN: 0301-0163.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198312
AB 50 women complaining of **hirsutism** were investigated in order to establish an optimal strategy for **hirsutism** exploration. Basal hormonal evaluations were of great value, especially serum **testosterone** and, to a lesser degree, DHA-S and LH. LH response to LHRH stimulation appeared of little diagnostic value. ACTH **stimulation** tests may be useful in detecting **enzyme** deficiencies in patients with normal basal values. The origin of hyperandrogenism can hardly be detected by the inhibition tests. However, these tests allow to determine whether the **androgen** secretion is still under ACTH and/or LH control.

L66 ANSWER 17 OF 20 MEDLINE
AN 82168091 MEDLINE
DN 82168091
TI 3 alpha, 17 beta-androstanediol glucuronide in plasma. A marker of **androgen** action in idiopathic **hirsutism**.
AU Horton R; Hawks D; Lobo R
NC AM13710 (NIADDK)

SO JOURNAL OF CLINICAL INVESTIGATION, (1982 May) 69 (5) 1203-6.
Journal code: HS7. ISSN: 0021-9738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198208
AB Biologically active **androgens** and peripheral **androgen** metabolites in plasma were measured in 25 women with idiopathic **hirsutism** (IH). Plasma **testosterone** was not significantly elevated. Free **testosterone** however was increased although the elevation was not impressive (10.9 +/- 6.6 SD vs. 3.3 +/- 1.5 ng/dl) and one-fourth of the cases had normal unbound **testosterone**. Dihydrotestosterone (DHT) values were elevated (23.5 +/- 14 vs. 12.5 +/- 3.59) but again over half of the values were within the normal range. In our series of mild to moderate cases, 3 alpha-diol was not at all discriminatory. However, plasma 3 alpha-diol glucuronide was markedly increased (604 +/- 376 vs. 40 +/- 10 ng/dl), and elevated in all but one mild case. Previous studies document that DHT is the important **androgen** in skin and formation of DHT and 3 alpha-diol is markedly increased in vitro in IH. Since 3 alpha-diol glucuronide is derived largely from extrasplanchnic events, beta-glucuronidase is present in skin, and **androgen** **stimulates** formation of the **enzyme** in extrasplanchnic tissue, we conclude that 3 alpha-diol glucuronide is a marker of peripheral **androgen** action and markedly elevated in IH.

L66 ANSWER 18 OF 20 MEDLINE
AN 80249813 MEDLINE
DN 80249813
TI Adrenocortical 11 beta-hydroxylation defect in adult women with postmenarchial onset of symptoms.
AU Cathelineau G; Brerault J L; Fiet J; Julien R; Dreux C; Canivet J
SO JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM, (1980 Aug) 51 (2) 287-91.
Journal code: HRB. ISSN: 0021-972X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198012
AB Four cases in adults of a deficiency in the 11 beta-hydroxylation of corticosteroids were investigated by both basal and dynamic biological studies. Symptoms varied from patient to patient; **hirsutism**, menstrual disturbance, acne, deepening of the voice, and arterial hypertension appeared post puberty. Basal testing demonstrated elevated levels of plasma **androgens**. These include delta 4-androstenedione (patients, 3.80-6.43 ng/ml; normal, 1.33 +/- 0.33 ng/ml), urinary 17-ketosteroids (patients, 11.8-16.7 mg/24 h; normal, 5-10 mg/24 h), and urinary dehydroepiandrosterone. The basal tests were often insufficient to show the accumulation of the precursors (especially 17-hydroxyprogesterone) which are often given as evidence for an increase in ACTH stimulation. In studying the levels of the mineralocorticoids, there was shown to be an increased basal level of tetrahydrodeoxycorticosterone (patients, 142-317 microgram/24 h; normal, 60-80 microgram/24 h) which was raised by ACTH

stimulation. These results, therefore, confirm the characteristic partial **enzyme** defect and give evidence for the heterogeneity of this syndrome. Based on the above observations, we believe it is appropriate to rename this condition adult adrenocortical 11 beta-hydroxylation defect rather than late-onset congenital adrenal hyperplasia.

L66 ANSWER 19 OF 20 MEDLINE
AN 75170445 MEDLINE
DN 75170445
TI Adrenal function in **hirsutism** I. Diurnal change and response of plasma androstenedione, **testosterone**, 17-hydroxyprogesterone, cortisol, LH and FSH to dexamethasone and 1/2 unit of ACTH.
AU Givens J R; Andersen R N; Ragland J B; Wiser W L; Umstot E S
SO JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM, (1975 Jun) 40 (6) 988-1000.
Journal code: HRB. ISSN: 0021-972X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 197510
AB ACTH dependency of plasma androstenedione (A) and **testosterone** (T) was determined in normal and **hirsute** women by measuring the magnitude of change of A and T between the time of the cortisol (F) peak and F nadir in a diurnal study. There was a significant diurnal rhythm of A synchronous with F in both normal and **hirsute** women (P less than 0.01). Five of 12 **hirsute** women had a greater than normal diurnal swing of A (P less than 0.05), but only 2 of the 12 had a greater than normal diurnal swing of T. Responsiveness of A and T to 1/2 unit of intravenous ACTH was determined after dexamethasone 1 mg was given the night before. Plasma A and T were elevated in most of the **hirsute** women during acute ACTH suppression by dexamethasone, indicating ACTH-independent hypersecretion of **androgens**. Nine of 17 **hirsute** women had a greater than normal A response to ACTH (P less than 0.05). Those who had an exaggerated diurnal swing of A also had hyper-responsiveness of A secretion to ACTH. Only 2 **hirsute** women had an exaggerated T response to ACTH. Some T levels were decreased by ACTH. Seven of the 9 hiruste women who had an exaggerated A response to ACTH had a normal maximum F response, but a greater than normal 17-hydroxy-progesterone (17-OHP) response to ACTH with a high 17-OHP to F ratio, suggesting they have a mild but compensated reduction in 21-hydroxylase or 11beta-hydroxylase activity. Two women with hyper-responsiveness of A secretion had low F and 17-OHP responses to ACTH suggesting reduced C21 but intact C19 3beta-hydroxysteroid dehydrogenase-delta-5,-4 isomerase activity. These apparent reduced **enzyme** activity may not be congenital, but **induced** by an altered hormonal milieu such as an abnormal **androgen** -estrogen ratio. It is concluded that ACTH uniformly stimulated A secretion but not T secretion and that approximately 50% of the **hirsute** women had ACTH-dependent hypersecretion of A, but most of these also had concurrent ACTH-independent hypersecretion of **androgens**.

L66 ANSWER 20 OF 20 MEDLINE
AN 75161591 MEDLINE

DN 75161591
TI **Testosterone** 5alpha-reduction in the skin of normal subjects and of patients with abnormal sex development.
AU Kuttenn F; Mauvais-Jarvis P
SO ACTA ENDOCRINOLOGICA, (1975 May) 79 (1) 164-76.
Journal code: 0NC. ISSN: 0001-5598.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197509
AB Human pubic skin was obtained from normal subjects and patients with abnormal sex differentiation. Skin samples (200 mg) supplemented with NADPH, were incubated for 1 h with labelled **testosterone**. The conversion of **testosterone** to dihydrotestosterone, 3alpha- and 3beta-androstanediol was calculated. This conversion averaged 14.9 plus or minus 3.4% (SE) in 11 normal men and 3.6 plus or minus 1.4% (SE) in 8 normal women. In 4 children as in 4 young hypogonadotrophic hypogonadal men, the conversion rate of **testosterone** to 5alpha-reduced metabolites was low (0.8 to 3.5%) and increased at puberty (13.5 to 19.2%). After administration of HCG for 3 months to 1 of the hypogonadal men, it reached 30.2%. Inversely, the formation of dihydrotestosterone and androstanediols from **testosterone** was suppressed in 2 men treated with large doses of oestrogen. In 3 subjects with an incomplete form of testicular feminization syndrome, the conversion rate of **testosterone** to 5alpha-reduced metabolites was in the normal male range (6.4 to 18.3%), whereas it was low in one case of the complete form of the syndrome (1.5%). In 9 women with idiopathic **hirsutism** the rate of 5alpha-reduced metabolites recovered from **testosterone** was close to that of normal men (13.5 plus or minus 5.5% (SE). From these results, it is postulated that in human subjects, there is a good correlation between **hair** growth in skin from a sexual area and the extent of **testosterone** 5alpha-reduction in this tissue. Such an **enzymatic** activity might be **induced** by active **androgens**; this latter hypothesis is in good agreement with the increase of 5alpha-reduction activity observed at puberty or after treatment of young hypogonadal males. In addition, it is pointed out that a positive correlation is observed between the 5alpha-reductase activity present in each skin sample studied and the urinary 3alpha-androstanediol found for the same individual. This confirms our previous findings suggesting that the determination of urinary 3alpha-androstanediol might prove of clinical interest in the evaluation of the **androgenic** status in human subjects.

=> d 1-13 bib abs

L68 ANSWER 1 OF 13 BIOSIS COPYRIGHT 1998 BIOSIS
AN 98:453425 BIOSIS
DN 01453425
TI Effects of valproate, phenobarbital, and carbamazepine on sex steroid setup in women with epilepsy.
AU Murialdo G; Galimberti C A; Gianelli M V; Rollero A; Polleri A; Copello F; Magri F; Ferrari E; Sampaolo P; Manni R; Tartara A
CS Dipartimento di Scienze Endocrinologiche e Metaboliche, Universita di Genova, Viale Benedetto XV, 6, I-16132 Genova, Italy
SO Clinical Neuropharmacology 21 (1). 1998. 52-58. ISSN: 0362-5664
LA English
AB Serum levels of sex-hormones, sex-hormone binding globulin, gonadotropin, and prolactin were evaluated during the follicular and the luteal phases in 65 women with epilepsy and in 20 healthy controls. Twenty-one patients were treated with sodium valproate (VPA), 21 with phenobarbital (PB), and 23 with carbamazepine (CBZ). VPA does not **stimulate** liver microsome **enzymes**, whereas PB and CBZ do. Patients on VPA therapy showed higher body weight and body mass index, but no significant differences in **hirsutism** score, or in ovary volume or polycystic ovary prevalence (at ultrasound examination). Estradiol levels were lower in all patient groups than in healthy controls in the follicular but not in the luteal phases. VPA affected luteal progesterone surge in 63.6% of cases. This effect was significantly lower in the CBZ and PB groups. Furthermore, increases in **testosterone** and A4-androstenedione levels and in free **androgen** index, along with a higher luteinizing hormone-follicle-stimulating hormone ratio in the luteal phase, were observed in women treated with VPA. Although sex-hormone binding globulin levels were higher in CBZ and PB than in VPA-treated patients, the differences were not significant because of the wide dispersion of the carrier protein levels. Inducer antiepileptic drugs decreased dehydroepiandrosterone sulfate levels, which remained unchanged during VPA treatment. No significant differences occurred in basal gonadotropin and prolactin levels.

L68 ANSWER 2 OF 13 WPIDS COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 97-108746 [10] WPIDS
DNC C97-034685
TI Compsn. for increasing **hair** growth, used esp. to treat male pattern baldness - comprises anti-**androgen**, co-**enzyme** Q and acetyl carnitine, opt. with **stimulator** of adenylate cyclase, penetrant and other additives.
DC B05 D21 E19
IN CRANDALL, W T
PA (CRAN-I) CRANDALL W T
CYC 22
PI WO 9702041 A1 970123 (9710)* EN 23 pp
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU BR CA JP MX
AU 9664825 A 970205 (9721)
ADT WO 9702041 A1 WO 96-US11270 960703; AU 9664825 A AU 96-64825 960703
FDT AU 9664825 A Based on WO 9702041
PRAI US 96-676095 960702; US 95-842 950703; US 95-5643 951019
AN 97-108746 [10] WPIDS
AB WO 9702041 A UPAB: 970307

Compsn. for increasing **hair** growth comprises an anti-**androgen**, coenzyme Q and acetyl carnitine.

The compsn. may include a stimulator of adenylate cyclase, a penetrant, a preservative, an antimicrobial, a gelling agent and an aroma-improving agent.

USE - The compsn. is used to increase **hair** growth, esp. to treat **androgenic alopecia** (male pattern baldness). The compsn. also increases **hair** lustre and decreases greying of the **hair**.

Dwg.0/0

L68 ANSWER 3 OF 13 BIOSIS COPYRIGHT 1998 BIOSIS
AN 97:33140 BIOSIS
DN 99339543
TI Effect of finasteride on human testicular steroidogenesis.
AU Castro-Magana M; Angulo M; Fuentes B; Canas A; Sarrantonio M; Arguello R; Vitollo P
CS Div. Endocrinol., Dep. Pediatrics, Winthrop-Univ. Hosp., 120 Mineola Blvd., Suite 210, Mineola, NY 11501, USA
SO Journal of Andrology 17 (5). 1996. 516-521. ISSN: 0196-3635
LA English
AB We studied the testicular function and some **androgen**-mediated events in 22 males (16-30 years of age) with male pattern baldness that was treated with finasteride (10 mg once daily) for 2 years. Patients were evaluated every 3 months. Prostatic volume was determined in six subjects by endorectal ultrasound scans. Serum gonadotropin, prostate-specific antigen (PSA), and sex hormone levels were determined basally and periodically during the treatment period. Fourteen subjects underwent gonadal stimulation with human chorionic gonadotropin (hCG), and the gonadotropin response to gonadotropin releasing hormone (GnRH) was determined in eight subjects, prior to and after 2 years of therapy. Finasteride treatment resulted in an improvement in the male pattern baldness and prostatic shrinkage that was associated with an increase in serum **testosterone** levels (17.2 +- 2.5 vs. 26.3 +- 1.7 nmol/L) and a decrease in dihydrotestosterone (DHT) levels (1.45 +- 0.41 vs. 0.38 +- 0.10 nmol/L), causing a marked increase in that **testosterone**/DHT ratio. A significant increase in the serum levels of androstenedione (3.67 +- 0.49 vs. 7.05 +- 0.70 nmol/L) and estradiol (132 +- 44 vs. 187 +- 26 pmol/L) was also noted, whereas androstanediol glucoronide (33.3 +- 6.4 vs. 10.7 +- 4.5 pmol) and PSA (1.6 +- 0.6 vs. 0.4 +- 0.1 ng/ml) were significantly decreased. No changes in basal or stimulated levels of gonadotropin were observed. There was a significant increase in the **testosterone** response to hCG during finasteride therapy (A: 16.7 vs. 35.5 nmol/L) that could be explained, at least in part, by the reduction of **testosterone** metabolism resulting from the blockage induced by finasteride. The decrease in the androstenedione to **testosterone** and estrone to estradiol ratios observed after hCG treatment, however, strongly suggests **increased** activity of the 17-ketosteroid reductase **enzyme** and an improvement of the testicular capacity for **testosterone** production.

L68 ANSWER 4 OF 13 BIOSIS COPYRIGHT 1998 BIOSIS
AN 94:551161 BIOSIS
DN 98010709
TI The effects of finasteride (Proscar) on **hair** growth, **hair** cycle stage, and serum **testosterone** and

dihydrotestosterone in adult male and female stumptail macaques (Macaca arctoides).
AU Rhodes L; Harper J; Uno H; Gaito G; Audette-Arruda J; Kurata S; Berman C; Primka R; Pikounis B
CS Dep. Endocrine Pharmacol., Merck Research Lab., RY80Y-140, P.O. Box 2000, Rahway, NJ 07065-0900, USA
SO Journal of Clinical Endocrinology & Metabolism 79 (4). 1994. 991-996. ISSN: 0021-972X
LA English
AB Finasteride, a 5-alpha-reductase inhibitor, was administered orally (i mg/ kg cntdot day) for 6 months to six male and five female stumptail macaques. Vehicle was given to five male and five female animals over the same period of time. **Hair** weights in a defined 1-in.2 area of frontal scalp were measured periodically every 1-2 months, and serum was collected for measurement of **testosterone** and dihydrotestosterone. In addition, scalp biopsies were taken before and 6 months after treatment to evaluate the micromorphometry of **hair** follicles. Results showed that both male and female serum dihydrotestosterone levels were significantly reduced (60-70%) by finasteride treatment. Both males and females showed statistically significant increases in mean **hair** weight over the treatment period compared to controls (P = 0.034). In addition, there was a statistically significant increase in mean follicle length (measured histologically in scalp biopsies) compared to baseline in the finasteride-treated animals (P = 0.028). These data show that an inhibition of 5a-reductase in the stumptail macaque can reverse the balding seen with age in both the male and female animals.

L68 ANSWER 5 OF 13 BIOSIS COPYRIGHT 1998 BIOSIS
AN 92:256528 BIOSIS
DN BA93:132853
TI INVESTIGATION OF ADRENAL FUNCTION IN WOMEN WITH OLIGOMENORRHOEA AND **HIRSUTISM** CLINICAL PCOS FROM THE NORTHEAST OF ENGLAND USING AN ADRENAL STIMULATION TEST.
AU TURNER E I; WATSON M J; PERRY L A; WHITE M C
CS DEP. CLIN. BIOCHEM., ROYAL INFIRMARY EDINBURGH, LAURISTON PLACE, EDINBURGH EH3 9YW, UK.
SO CLIN ENDOCRINOL 36 (4). 1992. 389-397. CODEN: CLECAP ISSN: 0300-0664
LA English
AB Objective: To determine the prevalence of adrenal enzyme dysfunction in women presenting with oligomenorrhoea and **hirsutism**, two clinical features of polycystic ovary syndrome (PCOS). Design: A prospective study of women attending outpatient clinics with these complaints. Androstenedione, dehydroepiandrosterone (DHEA), 17-hydroxyprogesterone (17-OHP), 11-deoxycortisol and cortisol were measured before and after overnight dexamethasone suppression and at 60 minutes after adrenal stimulation by ACTH injection. Subjects: Fifty women with clinical features of PCOS and 37 control women with regular cycles and normal **hair** distribution from the catchment area of the Royal Victoria Infirmary which includes Newcastle upon Tyne, Co. Durham, Cleveland, Cumbria and Northumberland. Measurements: Number of women with steroid responses to ACTH beyond the normal range, as defined by the responses of the control group and in previous studies. Results: Nineteen women (38%) were found to have some abnormality. One woman (2%) was identified with 21-hydroxylase (21-OHase) deficiency and a second (2%) had an increase in 17-OHP compatible with the heterozygote state for 21-OHase deficiency. Four women (8%) had isolated elevations in the

DHEA response consistent with minimal 3.beta.-hydroxysteroid dehydrogenase (3.beta.-HSD) deficiency. Thirteen women (26%) showed increases in both androstenedione and DHEA, or androstenedione alone, compatible with enhanced 17-20 lyase activity. Conclusions: Twelve per cent of the group showed evidence consistent with an adrenal **enzyme** deficiency; 26% had results in keeping with **increased** adrenal **androgen** production without an **enzyme** deficiency. These findings may be of relevance both in the pathogenesis of the features of PCOS and in determining appropriate treatment for individual patients.

L68 ANSWER 6 OF 13 BIOSIS COPYRIGHT 1998 BIOSIS
AN 92:171359 BIOSIS
DN BA93:93684
TI LATE-ONSET CONGENITAL ADRENAL HYPERPLASIA IN A GROUP OF HYPERANDROGENIC WOMEN.
AU HASSIAKOS D K; TONER J P; JONES G S; JONES H W JR
CS JONES INST. REPROD. MED., DEP. OBSTETRICS GYNECOL., EASTERN VA. MED. SCH., 825 FAIRFAX AVE., NORFOLK, VA. 23507.
SO ARCH GYNECOL OBSTET 249 (4). 1991. 165-172. CODEN: AGOBEJ ISSN: 0932-0067
LA English
AB The aim of this study was to determine the prevalence of late-onset congenital adrenal hyperplasia (LOCAH) in a group of hyperandrogenic women presenting with menstrual disturbances and/or infertility. Thirty-five women were evaluated by basal hormonal profiles and underwent ACTH stimulation testing. In this study, 17.1% of women showed evidence of partial 21-OH deficiency (21-OHD), and 5.7% 3.beta.-HSD deficiency. Neither basal hormonal levels nor clinical characteristics distinguished women with LOCAH from other hyperandrogenic women. And although the mean basal 17-OH progesterone (17-OHP) level in women with 21-OHD (152 .+-. 66 ng/dl) was significantly higher than levels in other **hirsute** women, 4 of 6 (67%) women with 21-OHD had normal 17-OHP levels. Thus, to identify all affected individuals with partial 21-OHD, our data suggest that hyperandrogenic women with basal unsuppressed 17-OHP levels > 100 ng/dl should undergo dynamic testing. With regard to partial 3.beta.-HSD deficiency, basal DHEA-S levels greater than the 95th percentile of other **hirsute** women may be used to screen for this deficiency. In conclusion, LOCAH due to partial steroid enzyme deficiencies are a frequent occurrence in women who present with symptoms of hyperandrogenism and ACTH stimulation remains an important tool in making make the diagnosis of enzyme deficiencies.

L68 ANSWER 7 OF 13 BIOSIS COPYRIGHT 1998 BIOSIS
AN 91:253339 BIOSIS
DN BA91:133894
TI EFFECTS OF KETOCONAZOLE IN **HIRSUTE** WOMEN.
AU AKALIN S
CS SECT. ENDOCRINOL., DEP. MED., HACETTEPE UNIV., SCH. MED., HACETTEPE, ANKARA 06100, TURKEY.
SO ACTA ENDOCRINOL 124 (1). 1991. 19-22. CODEN: ACENA7 ISSN: 0001-5598
LA English
AB To determine the efficacy of ketoconazole in the treatment of **hirsutism**, clinical and hormonal effects of this agent were evaluated with a randomized, placebo-controlled, double-blind cross-over study design. Nine **hirsute** women were given ketoconazole (600 mg/day) or placebo for 6 months and then crossed

over. The severity of **hirsutism** was assessed according to the scale of Ferriman & Gallwey. Baseline serum **testosterone**, dehydroepiandrosterone sulphate, progesterone, estradiol, basal and stimulated cortisol and 17-alpha hydroxyprogesterone were measured. Blood was also drawn for FSH and LH levels at 0, 30, 60, and 90 min of a GnRH stimulation test. The same parameters were determined following administration of placebo or ketoconazole for 6 months. The pretreatment (28.3.+-.0.9) and post-placebo (27.7.+-.1.4) Ferriman-Gallwey scores were significantly higher than the post-ketoconazole score (16.6.+-.1.3, p.ltoreq.0.01). Basal and stimulated cortisol levels were not blunted after ketoconazole, but basal and **stimulated** 17-hydroxyprogesterone levels were significantly higher, indicating sufficient **enzymatic** inhibition. Serum dehydroepiandrosterone sulphate and **testosterone** levels were significantly lowered following ketoconazole (p.ltoreq.0.05). Although E2 levels did not change significantly at any time, E2:**testosterone** ratios were significantly higher after ketoconazole (p.ltoreq.0.01), and the LH:FSH area ratio was also significantly greater than 3 after ketoconazole. It is concluded the ketoconazole significantly alleviates **hirsutism** by inhibiting steroid synthesis.

L68 ANSWER 8 OF 13 BIOSIS COPYRIGHT 1998 BIOSIS
AN 90:224329 BIOSIS
DN BA89:121619
TI INCREASE IN PLASMA 5-ALPHA ANDROSTANE-3-ALPHA 17-BETA-DIOL GLUCURONIDE AS A MARKER OF PERIPHERAL **ANDROGEN** ACTION IN **HIRSUTISM** A SIDE EFFECT INDUCED BY CYCLOSPORIN A.
AU VEXIAU P; FIET J; BOUDOU P; VILLETTE J-M; FEUTREN G; HARDY N; JULIEN R; DREUX C; BACH J-F; CATHELINEAU G
CS HOPITAL SAINT LOUIS, 1 RUE CLAUDE VELLEFAUX, 75475 PARIS CEDEX 10, FR.
SO J STEROID BIOCHEM 35 (1). 1990. 133-138. CODEN: JSTBBK ISSN: 0022-4731
LA English
AB Dose-dependent hypertrichosis is a common dermatological side-effect affecting the majority of patients treated with cyclosporine A (CSA). Previous studies have not demonstrated the influence of CSA on specific sex hormone levels. The aim of this study is to investigate whether CSA **increases** the activity of 5.alpha.-reductase, an **enzyme** which transforms **androgens** into dihydrotestosterone in peripheral tissues. The metabolite which best reflects this activity is 5.alpha.-androstane-3.alpha.,17.beta.-diol glucuronide (Adiol G). The study was carried out on 49 insulin-dependent diabetes patients participating in the double-blind "Cyclosporine-Diabete-France" clinical trial, of which 28 were treated with CSA (16 males and 12 females), and 21 received only placebo (10 males and 11 females). All patients underwent extensive clinical and laboratory evaluations prior to and during the present study. In addition to Adiol G, **testosterone** (T), dehydroepiandrosterone sulfate (DHEA S) and sex hormone-binding globulin (SHBG) were assayed. Levels of Adiol G increased significantly in CSA-treated groups: males, 11.86 .+-. 2.58 vs 7.83 .+-. 2.30 nmol/l; females, 4.48 .+-. 2.70 vs. 2.10 .+-. 1.22 nmol/l; $P < 0.02$ (comparison of means). There were no significant differences in this parameter before and during treatment in either the male or female placebo groups (paired t-test). During the treatment period, T, DHEA S, SHBG and the T/SHBG ratio did not significantly change with respect to their baseline values in any of the groups studied

(comparison of means). Comparison (using paired t-test) showed a significant increase of DHEA S in CSA-treated groups: males, .delta. = 3.08 nmol/l, P < 0.01; females, .delta. = 0.98 .+-. 1.13 nmol/l, P < 0.05. In conclusion, it is positive that CSA induces hypertrichosis or **hirsutism** by increasing 5.alpha.-reductase activity in peripheral tissues. Nevertheless the role of increased DHEA S as a possible Adiol G precursor cannot be excluded.

L68 ANSWER 9 OF 13 BIOSIS COPYRIGHT 1998 BIOSIS
AN 90:130503 BIOSIS
DN BA89:69314
TI LATE ONSET ADRENAL HYPERPLASIA IN A GROUP OF IRISH FEMALES WHO PRESENTED WITH **HIRSUTISM** IRREGULAR MENSES AND-OR CYSTIC ACNE.
AU MCLAUGHLIN B; BARRETT P; FINCH T; DEVLIN J G
CS BEAUMONT HOSP., BEAUMONT, DUBLIN 9, IRELAND.
SO CLIN ENDOCRINOL 32 (1). 1990. 57-64. CODEN: CLECAP ISSN: 0300-0664
LA English
AB The aims of this study were to determine the frequency of late-onset adrenal hyperplasia due specifically to 21-hydroxylase deficiency in a group of Irish women who presented at a Dublin Clinic with symptoms of hyperandrogenism, inlcuding **hirsutism**, menstrual irregularities and/or cystic acne, and to determine if those with 21-hydroxylase deficiency showed particular HLA associations. 119 women had blood samples taken basally and 1 h after an injection of 0.25 mg synacthen with the following hormones profiled: 17-hydroxyprogesterone, 11-deoxycortisol, androstenedione, **testosterone**, DHEAS and cortisol. Blood sampling was carried out between 0900 and 1000 h during the early follicular phase of the menstrual cycle (when applicable). Ninety-six subjects were new referrals to the Clinic for investigation of hyperandrogenism and 23 were acting as controls. In this study, 6% of patients showed evidence of partial 21-hydroxylase deficiency. In addition, 3 of 6 with partial 21-hydroxylase deficiency had normal baseline levels of 17-hydroxyprogesterone, with the biochemical abnormality becoming manifest only on synacthen stimulation. Late-onset adrenal hyperplasia due to partial deficiency of this enzyme should always be considered as a possible diagnosis in women who present with symptoms of hyperandrogenism. Syncthen **stimulation** is an important diagnostic tool in elucidating partial **enzyme** deficiency as baseline 17-hydroxyprogesterone may be normal in such patients.

L68 ANSWER 10 OF 13 BIOSIS COPYRIGHT 1998 BIOSIS
AN 89:309795 BIOSIS
DN BA88:23525
TI USEFULNESS OF KETOCONAZOLE NIZORAL IN THE TREATMENT OF **ANDROGENIZATION** SYMPTOMS IN WOMEN SUFFERING CONCURRENTLY FROM CANDIDIASIS OR DERMATOMYCOSIS.
AU KOVACS I; SZENDEI G; BERBIK I
CS FIRST DEP. OBSTET. GYNAECOL., SEMMELWEIS UNIV. MED. SCH., BUDAPEST.
SO THER HUNG 36 (4). 1988. 174-178. CODEN: THHUAF ISSN: 0133-3909
LA English
AB Ketoconazole (Nizoral) tablet has been used for the treatment of women suffering from symptoms of **androgenization**. Following therapy of some months significant decrease of the **androgenization** index and moderation of **hair** growth were observed besides the decrease of serum **testosterone** and serum cortisol levels and the **increase** of liver **enzyme** values. Though definite liver injury was observed in

these cases the author recommends the use of ketoconazole only in more severe cases.

L68 ANSWER 11 OF 13 BIOSIS COPYRIGHT 1998 BIOSIS
AN 84:309593 BIOSIS
DN BA78:46073
TI **ANDROGEN** METABOLISM IN **HIRSUTE** PATIENTS TREATED WITH CYPROTERONE ACETATE.
AU MOWSZOWICZ I; WRIGHT F; VINCENS M; RIGAUD C; NAHOUL K; MAVIER P; GUILLEMANT S; KUTTENN F; MAUVAIS-JARVIS P
CS SERVICE BIOCHIM., FAC. MED. PITIE-SALPETRIERE, 91 BD DE L'HOSP., 75634 PARIS CEDEX 13, FR.
SO J STEROID BIOCHEM 20 (3). 1984. 757-762. CODEN: JSTBBK ISSN: 0022-4731
LA English
AB Cyproterone acetate (CPA) in association with percutaneously administered estradiol was used for the treatment of 150 **hirsute** patients for periods ranging from 6 mo. to 3 yr. A spectacular clinical improvement ensued. Plasma **testosterone** (T) and androstenedione (A) fell from 69.0 .+-. 24 to 33.0 .+-. 8 and 210 .+-. 103 to 119 .+-. 25 ng/dl (mean .+-. SD), respectively, after 3 mo. of treatment and remained low thereafter. In contrast, T glucuronide (TG) and 3.alpha.-androstanediol (Adiol) remained high during the whole course of treatment: 37 .+-. 9 and 115 .+-. 43 .mu.g/24 h, respectively. In vitro T 5.alpha.-reductase activity (5.alpha.-R) in pubic skin decreased from 147 .+-. 34 t 79 .+-. 17 fmol/mg skin after 1 yr of treatment. To elucidate the discrepancy between plasma and urinary **androgen** levels, T production rate (PR) and metabolic clearance rate (MCR) were measured with the constant infusion technique in 7 patients before and after 6 mo. of treatment. PR decreased from 988 .+-. 205 to 380 .+-. 140 .mu.g/24 h (mean .+-. SD). In contrast MCRT increased from 1275 .+-. 200 to 1632 .+-. 360 1/24 h; this increase in MCRT explains the striking plasma T concentration fall and the high TG and Adiol excretion relative to the decrease in PR. Antipyrine clearance rate (no. = 8) increased from 36.3 .+-. 5.2 to 51.5 .+-. 7.4 ml/min while 6.beta.-hydroxycortisol remained unchanged. In conclusion, CPA acts through several mechanisms; it lowers the **androgen** input to the target cells by depressing T production through its antigonadotropic effect and accelerating T metabolic inactivation due to a partial **enzymatic inducer** effect on the liver; at the target cell level it competes with any remaining T for the receptor binding sites; the decrease in the **androgen**-dependent skin 5.alpha.-R is a consequence of both actions of **androgen** suppression and **androgen** receptor blockade; it reinforces the antiandrogenic effect of CPA.

L68 ANSWER 12 OF 13 BIOSIS COPYRIGHT 1998 BIOSIS
AN 82:295096 BIOSIS
DN BA74:67576
TI 3-ALPHA 17-BETA ANDROSTANEDIOL GLUCURONIDE IN PLASMA A MARKER OF **ANDROGEN** ACTION IN IDIOPATHIC **HIRSUTISM**.
AU HORTON R; HAWKS D; LOBO R
CS SECT. ENDOCRINOL., DEP. MED. OBSTET. GYNECOL., UNIV. SOUTHERN CALIF., SCH. MED., LOS ANGELES, CALIF. 90033.
SO J CLIN INVEST 69 (5). 1982. 1203-1206. CODEN: JCINAO ISSN: 0021-9738
LA English
AB Biologically active **androgens** and peripheral **androgen** metabolites in plasma were measured in 25 women with

idiopathic **hirsutism** (IH). Plasma **testosterone** was not significantly elevated. Free **testosterone**, however, was increased although the elevation was not impressive (10.9 .+-. 6.6 SD vs. 3.3 .+-. 1.5 ng/dl) and one-fourth of the cases had normal unbound **testosterone**. Dihydrotestosterone (DHT) values were elevated (23.5 .+-. 14 vs. 12.5 .+-. 3.59) but again over half of the values were within the normal range. In the series of mild to moderate cases, 3.alpha.-diol was not at all discriminatory. However, plasma 3.alpha.-diol glucuronide was markedly increased (604 .+-. 376 vs. 40 .+-. 10 ng/dl), and elevated in all but 1 mild case. Previous studies document that DHT is the important **androgen** in skin and formation of DHT and 3.alpha.-diol is markedly increased in vitro in IH. Since 3.alpha.-diol glucuronide is derived largely from extrasplanchnic events, .beta.-glucuronidase is present in skin, and **androgen stimulates** formation of the **enzyme** in extrasplachnic tissue, 3.alpha.-diol glucuronide apparently is a marker of peripheral **androgen** action and markedly elevated in IH.

L68 ANSWER 13 OF 13 BIOSIS COPYRIGHT 1998 BIOSIS
AN 81:131958 BIOSIS
DN BA71:1950
TI ADRENO CORTICAL 11-BETA HYDROXYLATION DEFECT IN ADULT WOMEN WITH POST MENARCHIAL ONSET OF SYMPTOMS.
AU CATHELINEAU G; BRERAULT J-L; FIET J; JULIEN R; DREUX C; CANIVET J
CS HOP. ST.-LOUIS, 1 PL. DU DR. ALFRED FOURNIER, 75475 PARIS CEDEX 10, FR.
SO J CLIN ENDOCRINOL METAB 51 (2). 1980. 287-291. CODEN: JCEMAZ ISSN: 0021-972X
LA English
AB Four cases in adults of a deficiency in the 11.beta.-hydroxylation of corticosteroids were investigated by both basal and dynamic biological studies. Symptoms varied from patient to patient; **hirsutism**, menstrual disturbance, acne, deepening of the voice and arterial hypertension appeared post puberty. Basal testing demonstrated elevated levels of plasma **androgens**. These include .DELTA.4-androstenedione (patients, 3.80-6.43 ng/ml; normal, 1.33 .+-. 0.33 ng/ml), urinary 17-ketosteroids (patients, 11.8-16.7 mg/24 h; normal, 5-10 mg/24 h) and urinary dehydroepiandrosterone. The basal tests were often insufficient to show the accumulation of the precursors (especially 17-hydroxyprogesterone) which are often given as evidence for an increase in ACTH stimulation. In studying the levels of the mineralocorticoids, there was an increased basal level of tetrahydrodeoxycorticosterone (patients, 142-317 .mu.g/24 h; normal, 60-80 .mu.g/24 h) which was raised by ACTH **stimulation**. The results confirm the characteristic partial **enzyme** defect and support the heterogeneity of this syndrome. Apparently it would be appropriate to rename this condition adult adrenocortical 11.beta.-hydroxylation defect rather than late-onset congenital adrenal hyperplasia.